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FIG. 1A

FIG. 1B

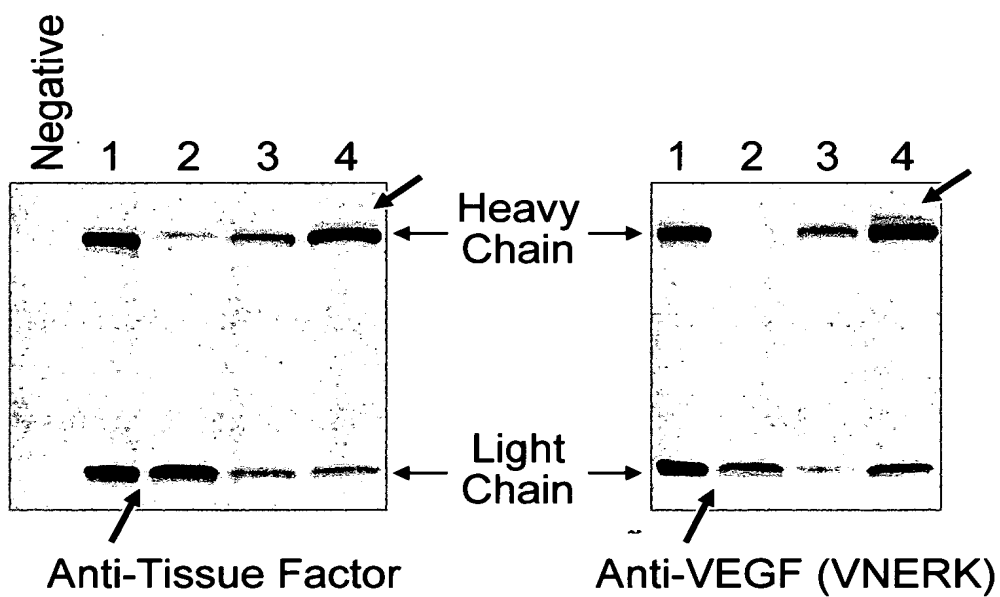


FIG. 2

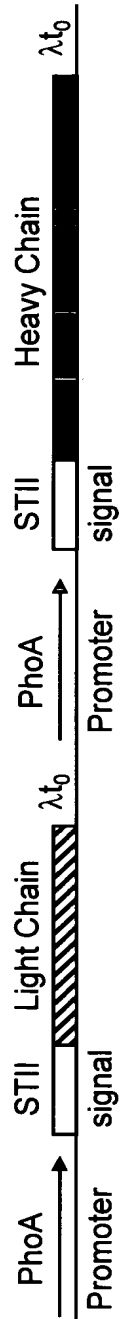


FIG. 3A

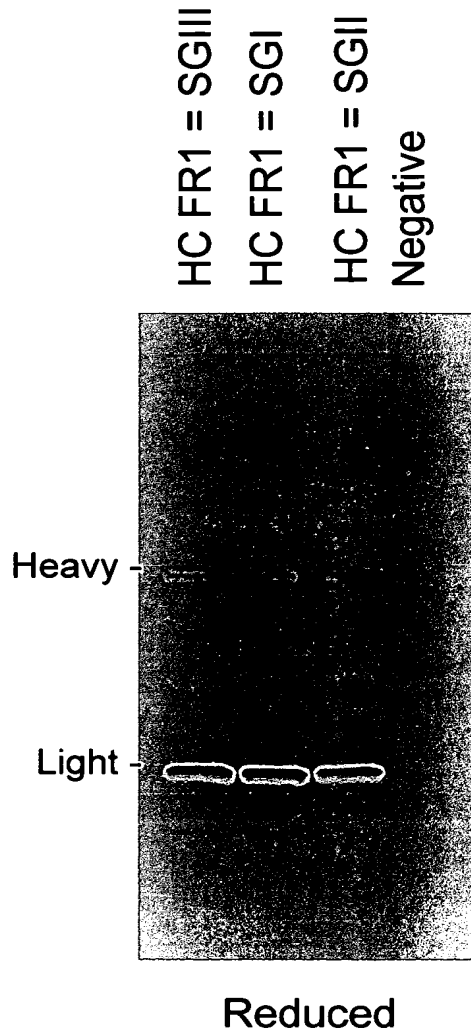


FIG. 3B

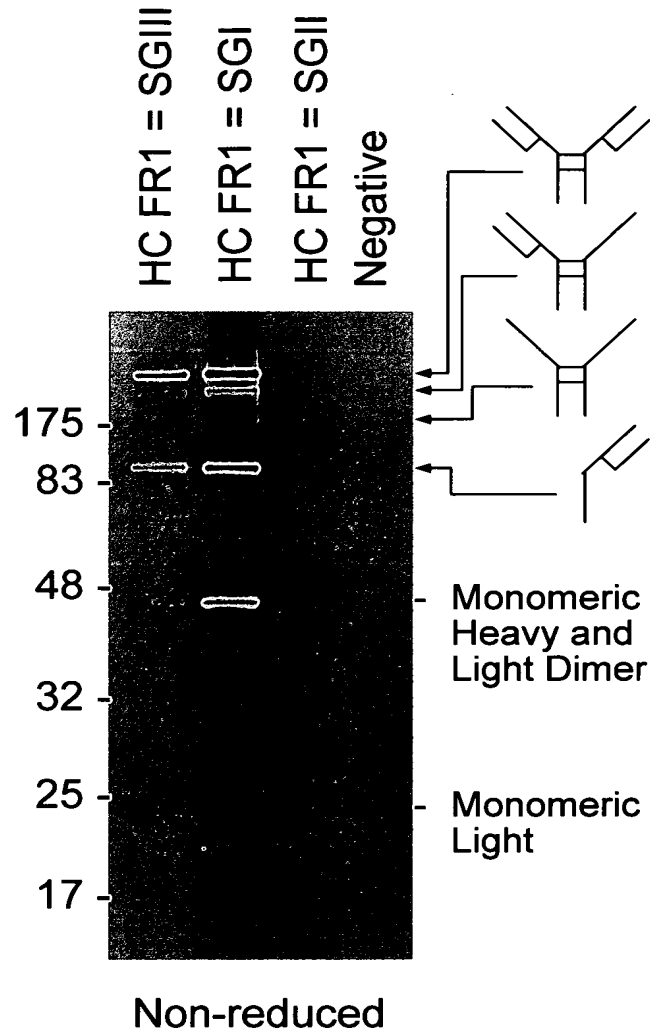


FIG. 4A

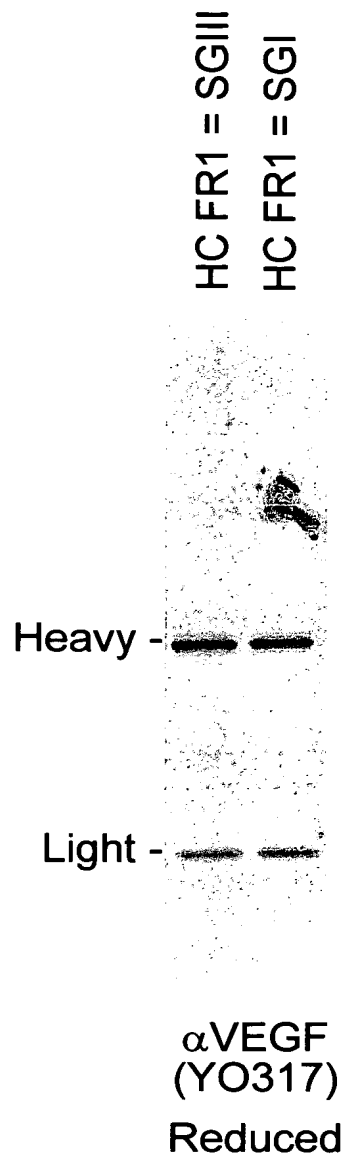


FIG. 4B

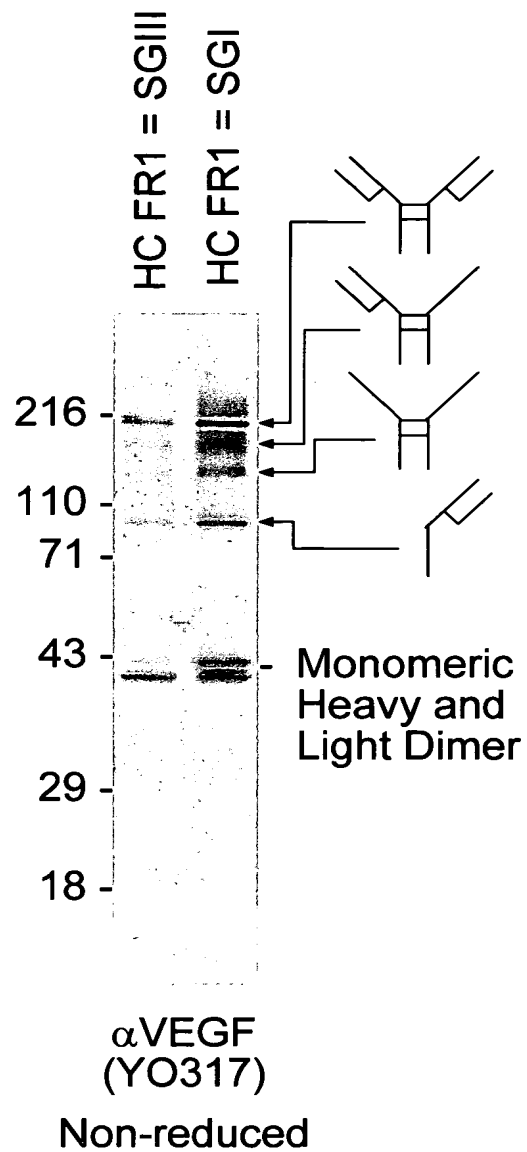
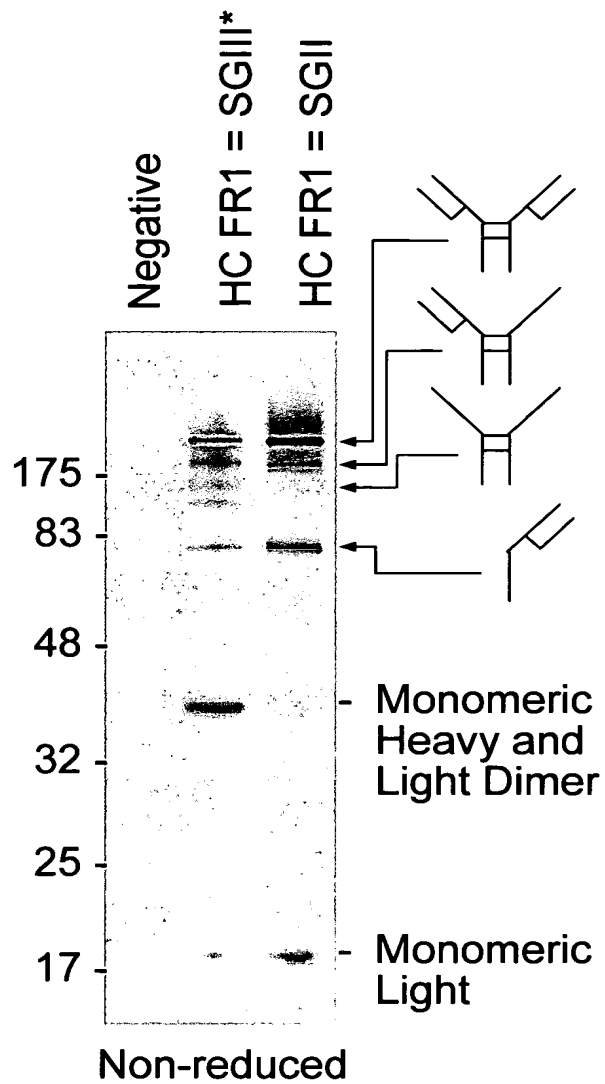


FIG. 5A



FIG. 5B



*Includes an A24V change as part of humanization.

FIG. 6A



FIG. 6B

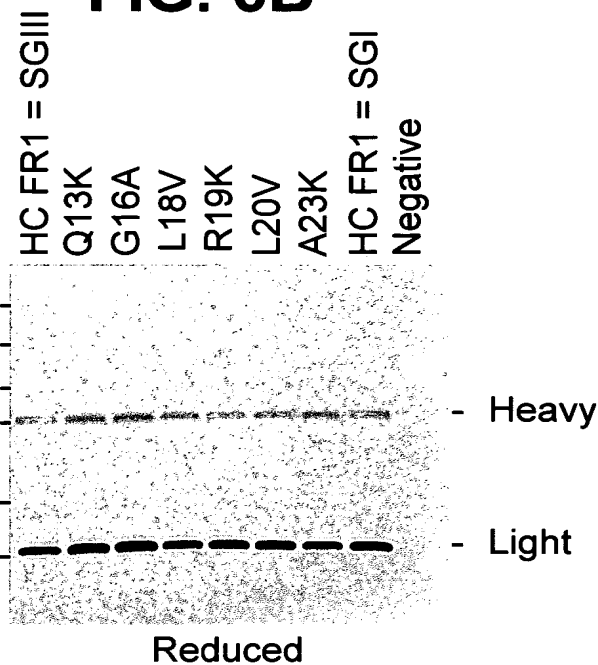


FIG. 6C

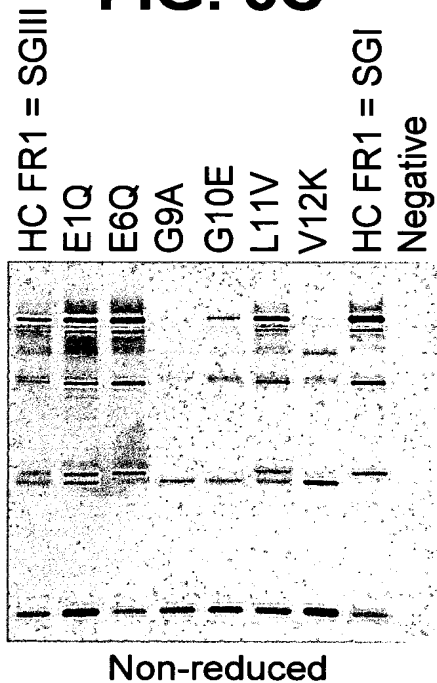


FIG. 6D

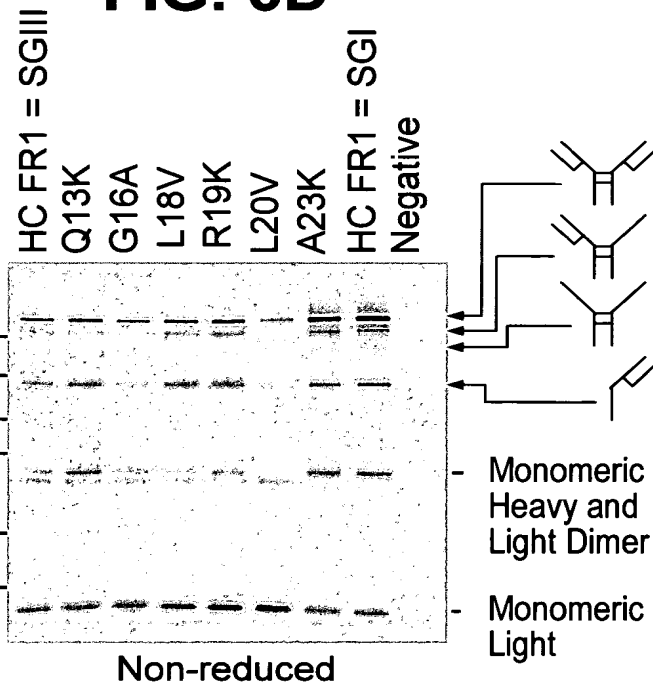


FIG. 7A

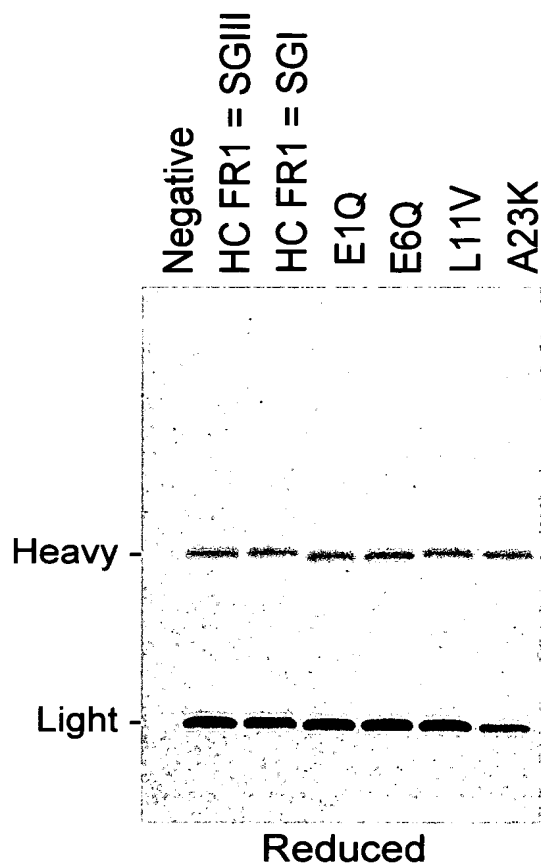


FIG. 7B

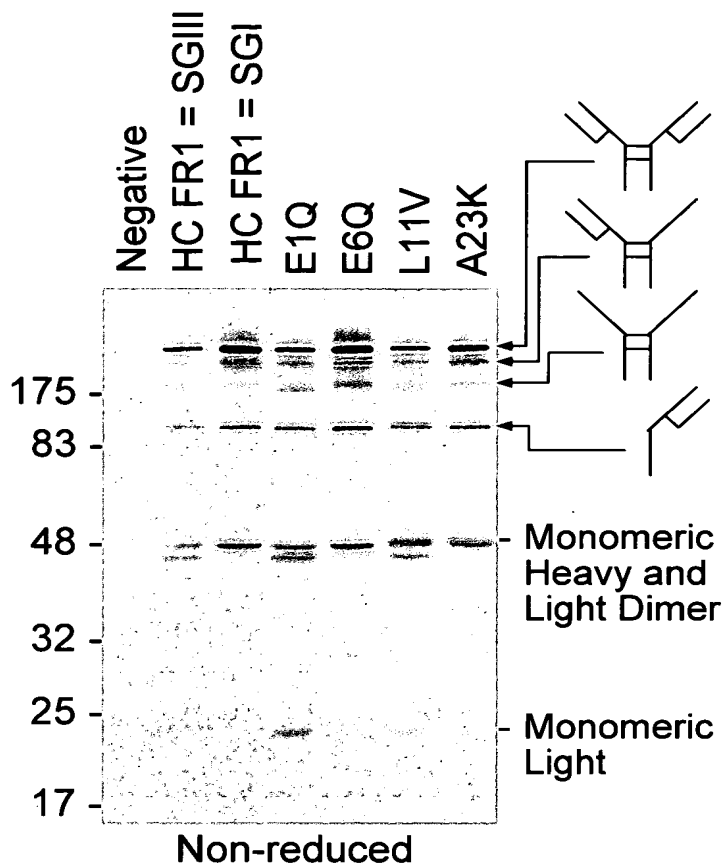


FIG. 8A

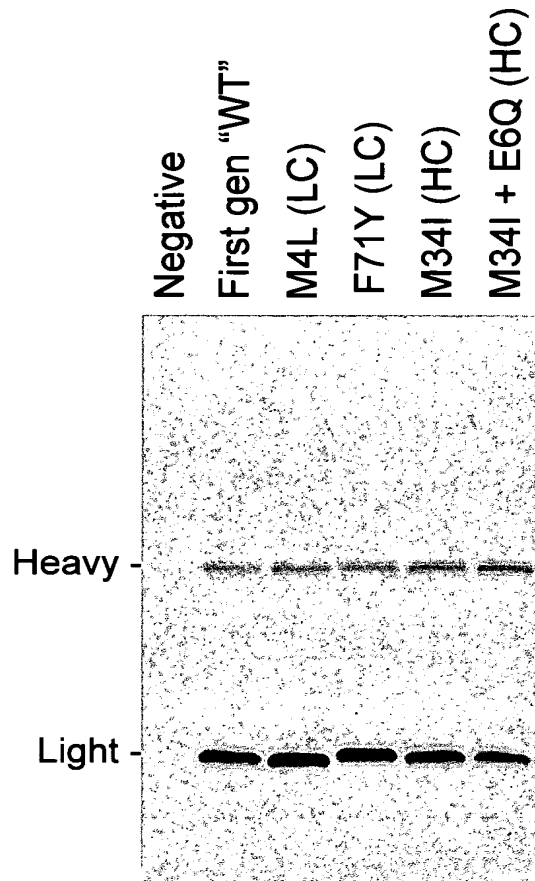


FIG. 8B

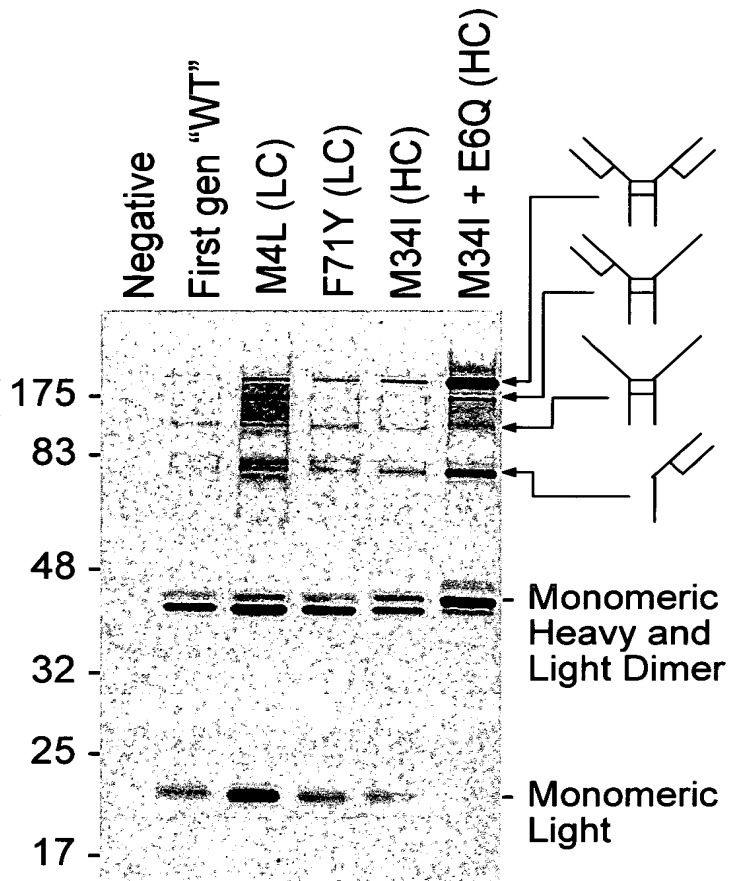


FIG. 9A

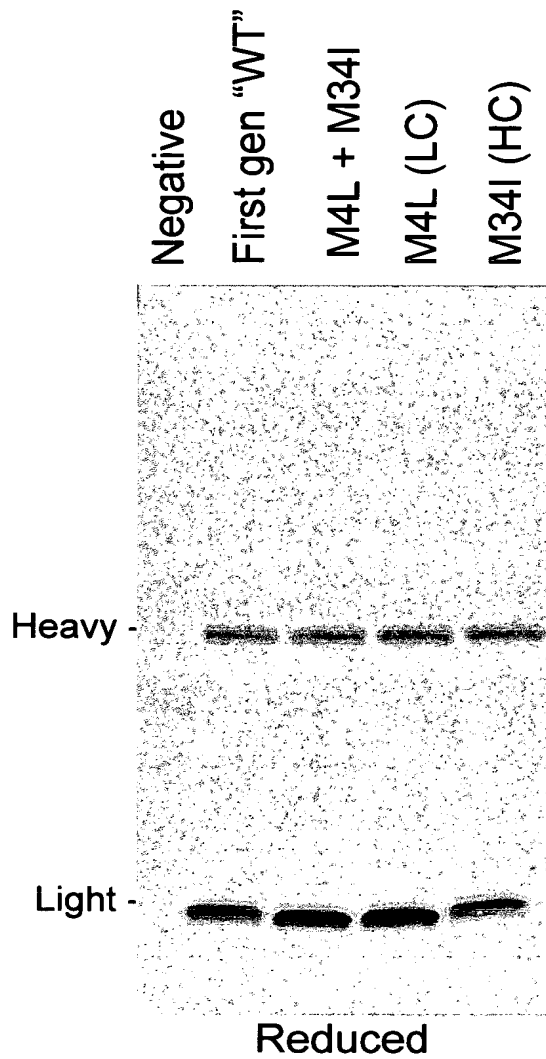


FIG. 9B

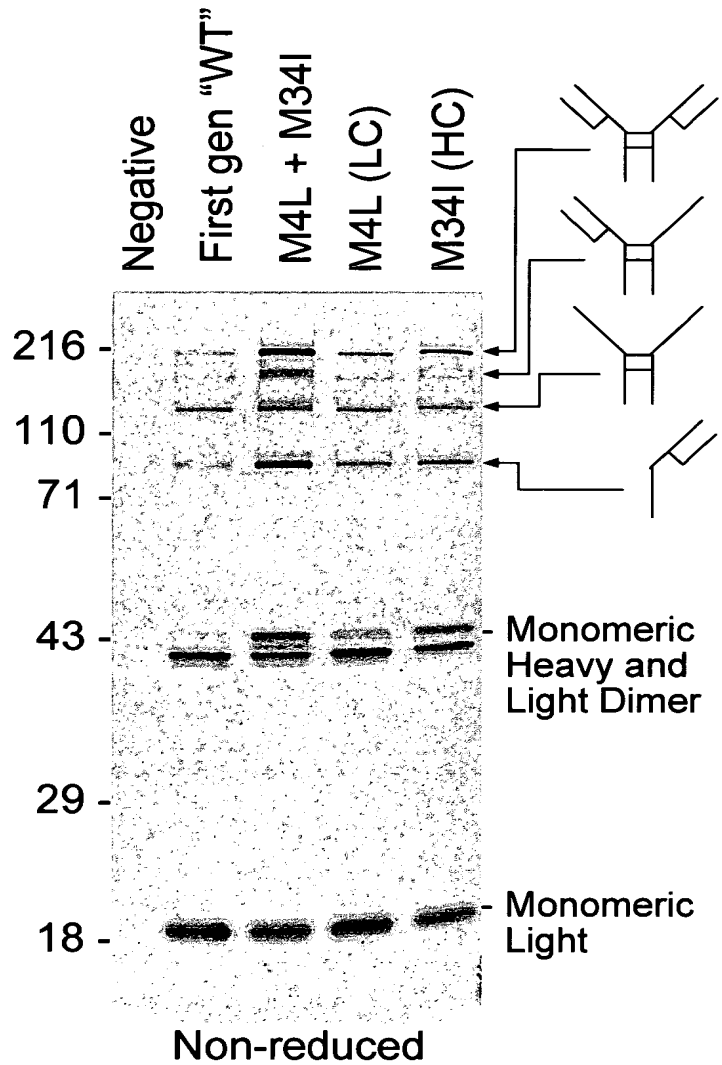


FIG. 10A

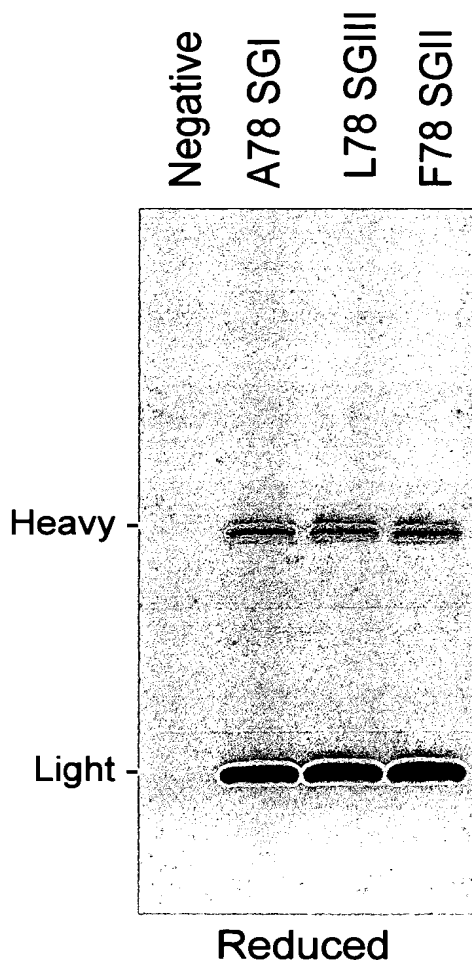


FIG. 10B

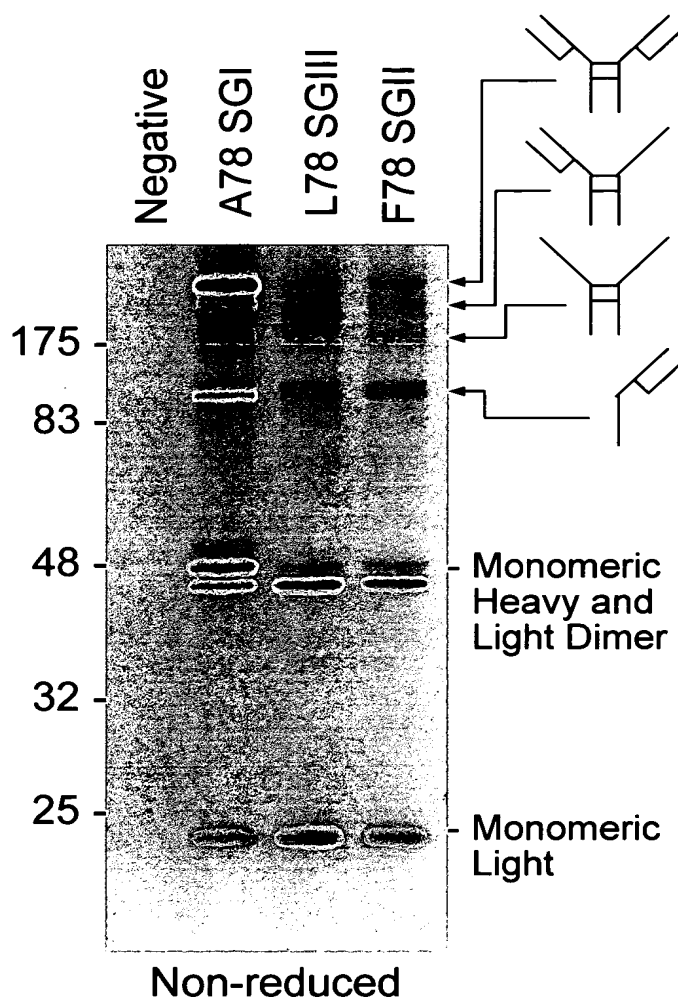


FIG. 11A

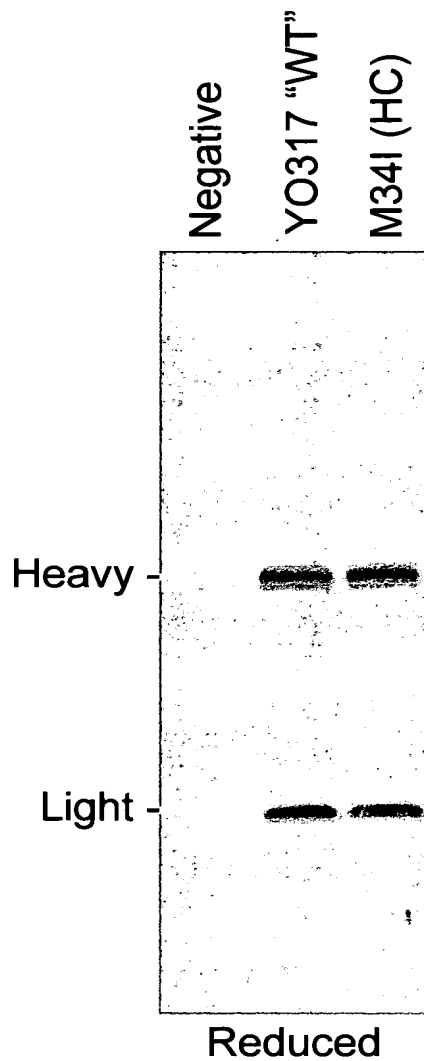


FIG. 11B

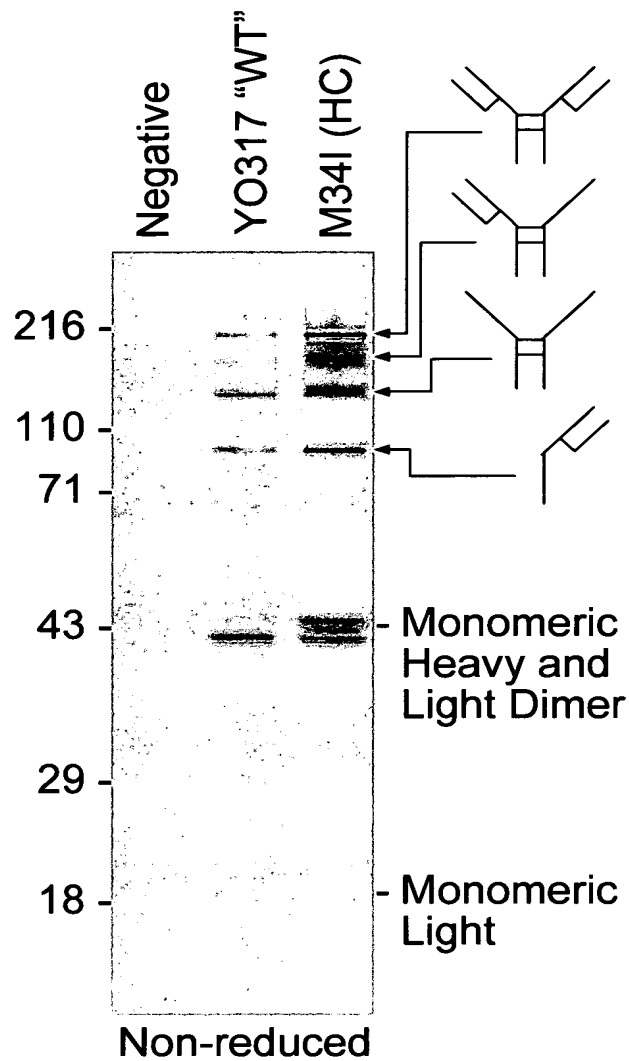


FIG. 12A

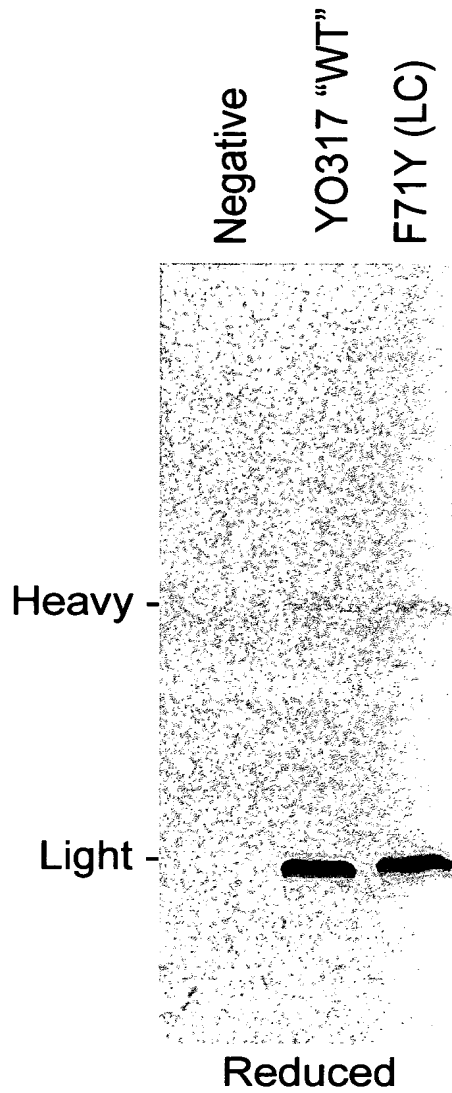


FIG. 12B

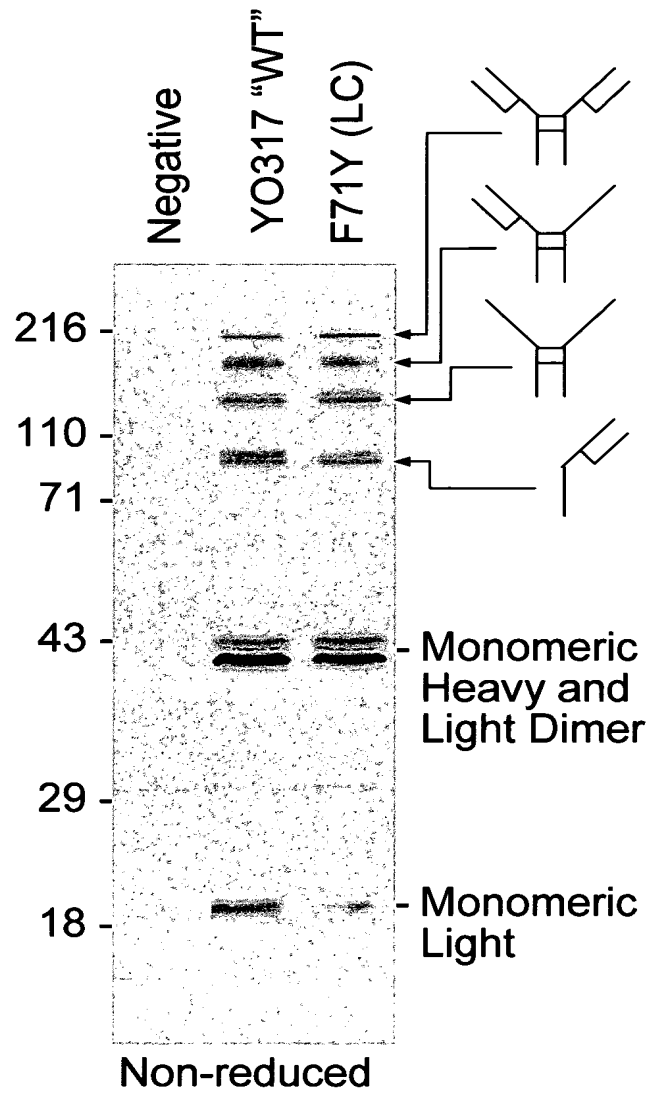


FIG. 13A

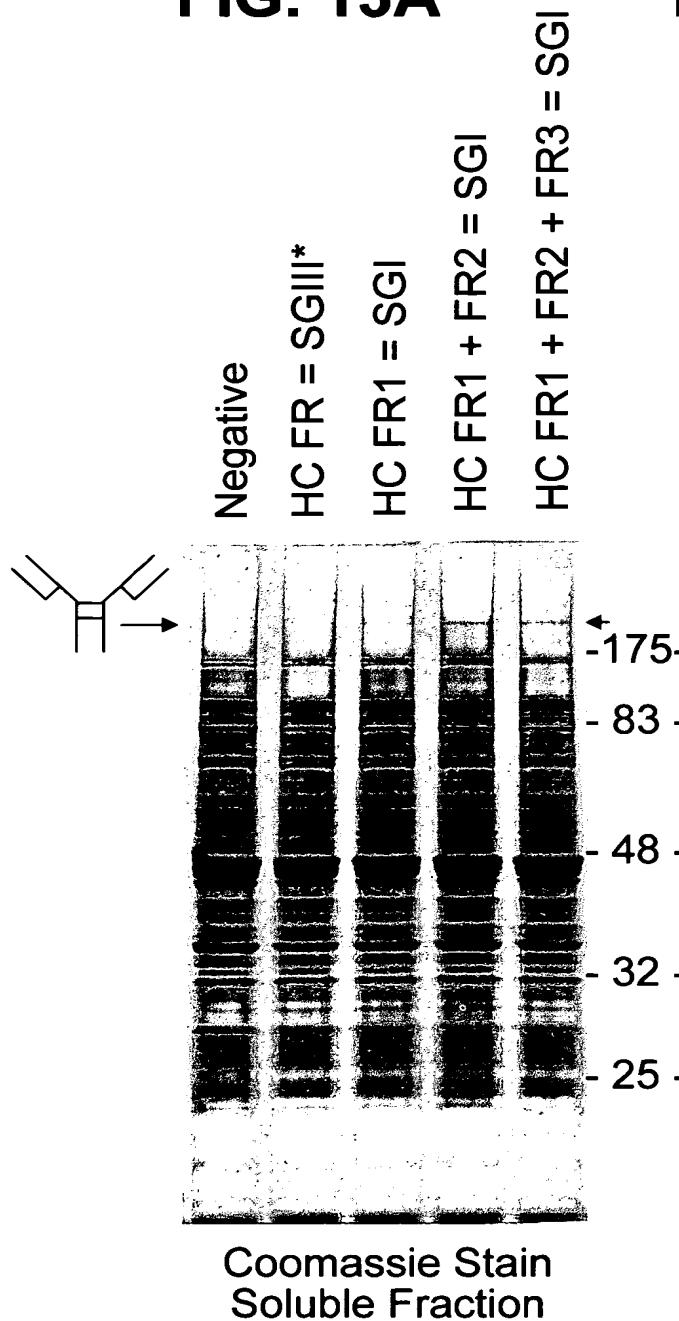
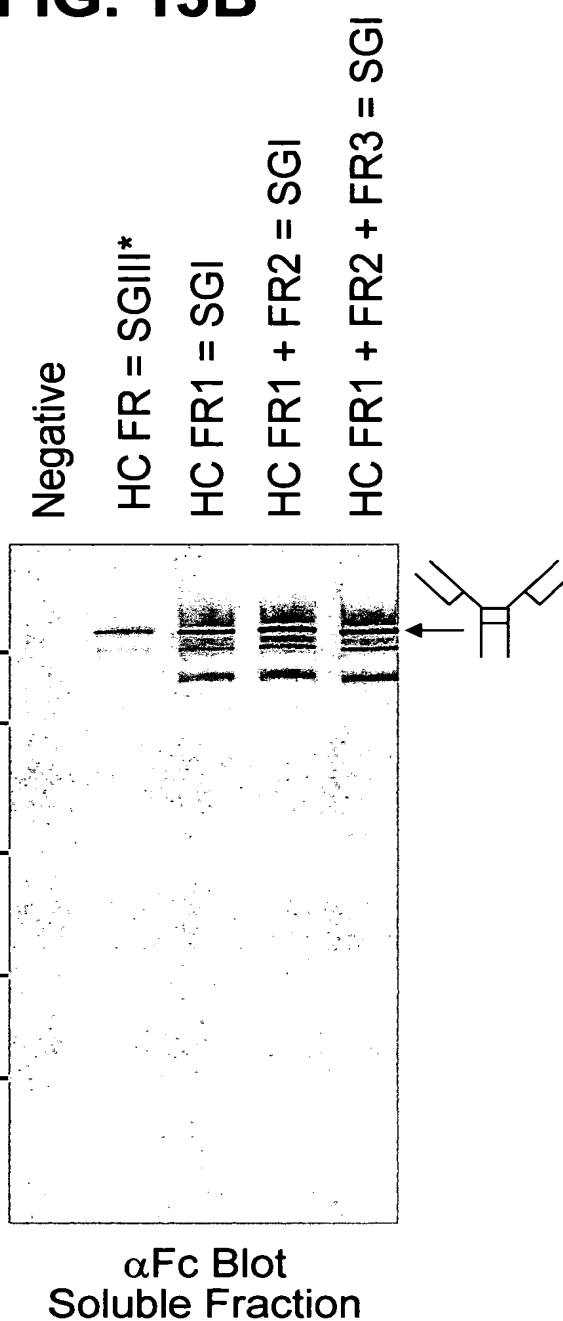


FIG. 13B



* Except for residues changed during humanization.

FIG. 14A

FIG. 14B

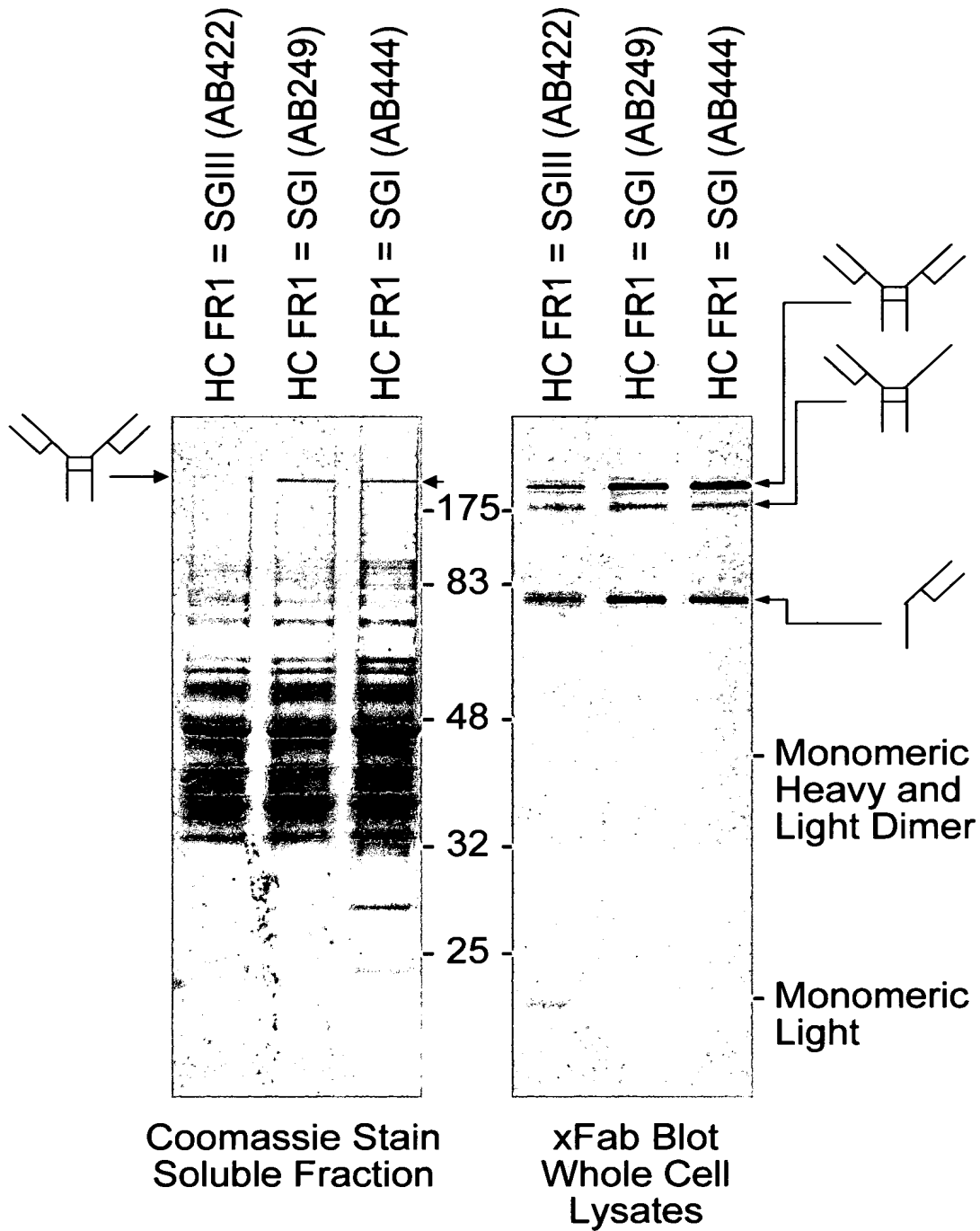




FIG. 15A

1 GAATTCAACT TCTCCATACT TTGGATAAGG AATACAGAC ATGAAAAATC TCATTGTCTG GTTGTATT TTTCGACGGG TTTTCTTCT TCTCAGCTTA
CTTAAGTTGA AGAGGTATGA AACCTATTCC TTTATGTCTG TACTTTTATG AGTAACGACT CAACAATAA TTGCAACGGG TTTTCTTCT TCTCAGCTTA

101 GAACTGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCTGTA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAGG
CTTGACACAC GCGTCCATCT TCGAAACCTC TAATAGCAGT GACGTTACGA AGCGTTATAC CGCGTTTAC TGGTTGTCCG CAACTAAC TA GTCCATCTCC

201 GGGCGCTGTA CGAGGTAAG CCGATGCCA GCATTCTGA CGACATACG GAGCTGTCTG GCGATTACGT AAAGAAGTTA TTGAAGCATC CTCGTCTAGTA
CCCGGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA TTTCTTCAAT AACTTCGTAG GAGCAGTCAT

301 AAAAGTTAAT CTTTCAACA GCTGTCATAA AGTTGTCAG GCGGACAT TCAACAGTGC CGGCTCTGAA TATCAGCGAA ACAAATAA AAAATTACAT AAACATTGAT CATCGCTTCA
TTTTCAATTA GAAAAGTTGT CGACAGTATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA ACAAATAA AAAATTACAT AAACATTGAT CATCGCTTCA

401 TCAGGTAAA AGGTATCTA GAATTATGAA GAAGATATC GCATTCTTC TTGCATCTAT GTTCGTTTTT TCTATTGCTA CAAACGCGTA CGCTGATATC
AGTGCAATTT TCCCATAGAT CTTAATACTT CTTCCTATAG CGTAAGAAG AAGCTAGATA CAAGCAAAA AGATAACGAT GTTTGGCAT GCGACTATAG

1 M K K N I A F L L A S M F V F S I A T N A Y A D I
^STII Signal TIR -1
anti-VEGF Light Chain^

501 CAGTTGACCC AGTCCCGAG CTCCCTGTCC GCCTCTGTGG GCGATAGGGT CACCATCACC TGCAGCGCAA GTCAGATAT TAGCAACTAT TTAACACTGGT
GTCAACTGGG TCAGGGGCTC GAGGACAGG CGGACACACC CGCTATCCCA GTGGTAGTGG ACGTCGCGTT CAGTCCTATA ATCGTTGATA AATTGACCA

26 Q L T Q S P S S L S A S V G D R V T I T C S A S Q D I S N Y L N W Y
^variable light (VL) cys

601 ATCAACAGAA ACCAGGAAA GCTCCGAAAG TACTGATTGA CTTCACTCC TCTCTCCACT CTGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGAC
TAGTTGTCTT TGGTCTCTTT CGAGGCTTTC ATGACTAAT ATGACTAAT GAAGTGAGG AGAGAGTGA GACCTCAGG AAGAGCGAAG AGACCTAGGC CAAGACCTGT

60 Q Q K P G K A P K V L I Y F T S S L H S G V P S R F S G S G T
^variable light cys

701 GGATTTCACT CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTGTA ACAGTATAGC ACCGTGCGGT GGACGTTTGG ACAGGTTACC
CCTAAAGTGA GACTGTTAGT CGTCAGACGT CGGTCTTCTG AAGCGTTGAA TAATGACAGT TGTATATCG TGGCAGGGA CCTGCAACC TGTCCTCATGG

93 D F T L T I S S L Q P E D F A T Y C Q Q Y S T V P W T F G Q G T
^Variable light cys

801 AAGTTGGAGA TCAACGAAC TGTGGCTGCA CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT GTGTGCTGTC
TTCCACCTCT AGTTTGTCTG ACACCGAGGT GGTAGACAGA AGTAGAAGG CGGTAGACTA CTCGTCAACT TTAGACCTTG ACGAAGACAA CACACGACG

126 K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V V C L L
Constant Light cys^

FIG. 15B

```
901 TGAATAACTT CTATCCAGA GAGGCCAAG TACAGTGAA GGTGATAAC GGCCTCAAT CGGTAACCTC CCAGGAGACT GTACACAGC AGGACAGCAA
ACTTATTGAA GATAGGTCT CTCCGGTTTC ATGTCACCTT CCACCTATTG CCGGAGGTGA GCCCTCTCTCA CAGTGTCTCG TCCTGTCTGT
160 N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K

1001 GGACAGCACC TACAGCCTCA GCAGCACCTT GACCTGAGC AAAGCAGACT ACAGAAACA CAAAGTCTAC GCCTCGGAAG TCACCCATCA GGGCCTGAGC
CCTGCTGTGG ATGTCGGAGT CGTCGTGGA CTGCACTCG TTTCGTCTGA TGCTCTTTGT GTTTCAGATG CCGAGCCTTC AGTGGTAGT CCGGAGACTCG
193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S
^Constant Light cys

1101 TCGCCCGTCA CAAAGAGCTT CAACAGGGGA GAGTGTAAAT TAAATCTCTT AGCCGGAGC CATCGTGGCG AGCTCGGTAC CCGGGGATCT AGGCTAAGC
AGCGGGCAGT GTTCTCTGAA GTTGTCCTCT CTCACAATTA ATTTAGGAGA TGCGGCTCTG GTAGCACCGC TCGAGCCATG GGCCCCCTAGA TCCGGATTGC
226 S P V T K S F N R G E C O
^cys to bind heavy

start lambda t0 terminator^

1201 CTCGGTTGCC GCCGGCGGTT TTTTATTGTT GCCGACGGC ATCTCGAATG AACTGTGTGC GCAGGTAGAA GCTTTGGAGA TTATCGTAC TGAATGCTT
GAGCCAACGG CGGCCGCAA AAATAACAA CCGCTGCGG TAGAGCTTAC TTACACACAG CGTCCATCTT CGAAACCTCT AATAGCAGTG ACGTTACGAA
^end lambda t0 terminator

1301 CGCATATGG CGCAAAATGA CCAACAGCGG TTGATTGATC AGGTAGAGG GCGCTGTCTAC GAGGTAAAG CCGATGCCAG CATTCCTGAC GACGATAGCG
CGGTTATACC GCGTTTACT GGTGTGCGC AACTAACTAG TCCATCTCCC CCGCGACATG CTCGATTTCG GGTACGGTC GTAAGGACTG CTGCTATGCC

1401 AGCTGCTGG CGATTACGTA AAGAAGTTAT TGAAGCATCC TCGTCAGTAA AAGTTAATC TTTTCAACAG CTGTCAATAA GTTGTCACGG CCGAGACTTA
TCGACGACGC GCTAATGCAAT TTCTTCAATA ACTTCGTAGG AGCAGTCAAT TTTCATTTAG AAAAGTTGTC GACAGTATTT CAACAGTGCC GGCTCTGAAT

1501 TAGTCGCTTT GTTTTATTT TTTAATGAT TTGTAACATG TACGCAAGTT CAGTAAAAA GGGTATCTAG AATTATGAAG AAGAATATCG CATTTCTTCT
ATCAGCGAAA CAAAAATAAA AAATTACATA AACATTGATC ATGCGTTCAA GTGCATTTTT CCCATAGATC TTAATACTTC TTCTTATAGC GTAAAGAAGA
M K K N I A F L L
^STII Signal TIR-1

1601 TGCATCTATG TTCGTTTTTT CTATTGCTAC AAACGCGTAC GCTGAGTTC AGCTGGTGA GTCTGGCGGT GGCTGGTGC AGCCAGGGG CTCACTCGT
ACGTAGATAC AAGCAAAAAA GATAACGATG TTTGCGCATG CGACTCCAAG TCAGCCACCT CAGACCGCCA CCGGACCAAG TCGGTCCCCC GAGTGAGGCA
10 A S M F V F S I A T N A Y A E V Q L V E S G G L V Q P G G S L R
^anti-VEGF heavy chain (VNERK version)

1701 TTGTCTGTG CAGCTTCTGG CTATACCTTC ACCAACTATG GTATAAATG GTTCCGTCAG GCCCGGGTA AGGGCTGGA ATGGGTGGA TGGATTAAAC
AACAGGACAC GTCGAAGACC GATATGGAAG TGGTTGATAC CATATTGAC CCAGGCAGTC CCGGGCCCAT TCCCGACCT TACCCACCT ACCTAATGT
43 L S C A A S G Y T F T N Y G I N W V R Q A P G K G L E W V G W I N T
^Variable Heavy (VH) cys

1801 CCTATACCG TGAACCGACC TATGCTGGG ATTTCAAAG TGTTCCTTCT TTTTCTTTAG ACACCTCAA AAGCACAGCA TACCTGCAGA TGAACGCCT
GGATATGCC ACTTGGCTGG ATAGACGCC TAAAGTTGC AGCAAGTGA AAAAGAAATC TGTGGAGTT TCGGTGTCTG ATGGAGCTCT ACTTGTGGA
77 Y T G E P T Y A A D F K R R F T F S L D T S K S T A Y L Q M N S L
```

FIG. 15C

1901 GCGGCGTGAG GACACTGCGG TCTATTACTG TGCAAAAGTAC CCGACTATT ATGTGAACGA GCGAAGAGC CACTGGTATT TGCAGCTGT GGTCAAGGA
CGCGGACTC CTGTGACGGC AGATAATGAC ACGTTTTCATG GCGGTGATAA TACACTTGCT CGCTTCTCG GTGACCATAA AGCTGCAGAC CCCAGTTCCT
110 R A E D T A V Y Y C A K Y P H Y Y V N E R K S H W Y F D V W G Q G
^VH cys

2001 ACCCTGGTCA CGTCTCTC GGCCTCCACC AAGGGCCCAT CGGTCTTCCC CCTGGCACCC TCCTCCAAGA GCACCTTGG GGGCACAGCG GCCTGGGCT
TGGGACCACT GGCAGAGGAG CCGGAGGTGG TTCCCGGGTA GCCAAGGG GGAACCTGGG AGAGGTTCCT CGTGGAGACC CCCGTGTGCG CCGGACCCGA
143 T L V T V S S A S T K G P S V F P L A P S S K S T S G G T A A L G C
Constant Heavy 1 (CH1) cys^

2101 GCCTGGTCAA GGACTACTTC CCCGAACCGG TGACGGTCTC GTGGAATCA GCGGCCCTGA CCAGCGGGT GCACACCTTC CCGGCTGTCC TACAGTCTC
CGGACCACTT CCTGATGAAG GGGCTTGGCC ACTGCCACAG CACCTTGAGT CCGCGGACT GTGCGCGCA CGTGTGAGG GCGCGACAG ATGTCAAGG
177 L V K D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S
^CH1 cys

2201 AGGACTCTAC TCCCTCAGCA GCGTGTGAC TGTGCCCTCT AGCAGCTGG GCACCCAGAC CTACATCTGC AACGTGAATC ACAAGCCCAG CAACACCAAG
TCCTGAGATG AGGGAGTCGT CGCACCACTG ACACGGGAGA TCGTGAACC CGTGGGTCTG GATGTAGACG TTGCACTTAG TGTTCGGTC GTTGTGGTTC
210 G L Y S L S S V V T V P S S L G T Q T Y I C N V N H K P S N T K
^CH1 cys

2301 GTGGACAAGA AAGTTGAGCC CAAATCTTGT GACAAACTC ACACATGCC ACCGTGCCCA GCACCTGAAC TCCTGGGGG ACCGTGAGTC TTCTCTTCC
CACCTGTTCT TTCAACTCGG GTTTAGAAC CTGTTTTCAG TGTGTACGG GTGCACGGT CGTGGACTG AGGACCCCC TGGCAGTCAG AAGGAGAGG
243 V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F L F P
^cys to bind light chain ^hinge cys

2401 CCCCCAACCA CAAGGACACC CTATGATCT CCCGGACCCC TGAGTCACTA TGGTGTGTGG TGGACGTGAG CCACGAAGAC CCTGAGGTCA AGTCAACTG
GGGGTTTTGG GTTCTGTGG GAGTACTAGA GGGCTGGGG ACTCCAGTGT ACGCACCACT ACGTGCATC GTGTCTCTG GGAATCCAGT TCAAGTTGAC
277 P K P K D T L M I S R T P E V T C V V V D V S H E D P E V K F N W
^Constant Heavy 2 (CH2) cys

2501 GTACGTGGAC GGGGTGGAGG TGCATAATGC CAAGACAAG CCGCGGGAGG AGCAGTACAA CAGCAGTAC CAGTGTGTCA GGTCTCTCAC CGTCTGAC
CATGCACCTG CCGCACCTCC ACGTATTACG GTTCTGTTC GTTCTGTTC GCGCCCTCC TCGTCATGTT GTCTGTGATG GCACACCACT CCGCAGGAGT GCAGGACGTG
310 Y V D G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H
^CH2 cys

2601 CAGGACTGSC TGAATGGCAA GGAGTACAAG TGCAGGTCT CCAACAAGC CCTCCCAAGC CCCATCGAGA AAACCATCTC CAAAGCCAAA GGGCAGCCCC
GTCTGACCG ACTTACCGTT CCTCATGTT C K K V S N K A L P A P I E K T I S K A K G Q P R
343 Q D W L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R
^CH2 cys

2701 GAGAACCA GGTGTACACC CTGCCCCCAT CCGGGGAAGA GATGACCAAG AACCAGTCA GCCTGACCTG CCTGTCAA GGTCTCTATC CCAGCGACAT
CTCTTGGTGT CCACATGTGG GACGGGGTA GGGCCCTTCT CTACTGTTT TGTGTCCAGT CCGACTGAC GGAACAGTTT CCGAAGATAG GGTGCGTGT
377 E P Q V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I
^Constant Heavy 3 (CH3) cys

FIG. 15D

```
2801 CGCCGTGGAG TGGGAGAGCA ATGGGCAGCC GGAGAACAAC TACAAGACCA CGCTCCCGT GCTGGACTCC GACGGCTCCT TCTTCTCTTA CAGCAAGCTC
    GCGGCACCTC ACCCTCTCGT TACCCGTCCG CCTCTTGTG ATGTTCTGGT GCGGAGGCA CGACCTGAGG CTGCCGAGGA AGAAGAGAT GTCGTTGAG
410 A V E W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L
2901 ACCGTGGACA AGAGCAGGTG GCAGCAGGG AACGTCTTCT CATGCTCCGT GATGCATGAG GCTCTGCACA ACCACTACAC GCAGAAGAGC CTCTCCCTGT
    TGGCACCTGT TCTCGTCCAC CGTCGTCCCC TTGCAGAAGA GTACGAGGCA CTACGTACTC CGAGACGTGT TGGTGATGTG CGTCTTCTCG GAGAGGGACA
443 T V D K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S
    ^CH3 cys
3001 CTCGGGTAA ATAAGCATGC GACGGCCCTA GAGTCCCTAA CGCTCGGTTG CCGCCGGGCG TTTTATTG TTAATCATG TTTGACAGCT TATCATCGAT
    GAGGCCCAT TATTCTGACG CTGCCGGGAT CTCAGGGATT GCGAGCCAAC GCGCGGCCCG AAAAAATAAC AATTGAGTAC AACTGTGA ATAGTAGCTA
477 P G K O
    ^start lambda t0 terminator ^end lambda t0 terminator
    ^start of tet resistance promoter ^start of tet resistance promoter
    ^-35 of promoter
3101 AAGCTTTAAT GCGGTAGTTT ATCACAGTTA AATTGCTAAC GCAGTCAGGC ACCGTGTATG AAATCTAACA ATGCCGTCAT CGTCATCCTC GGCACCGTCA
    TTGGAATTA CGCCATCAAA TAGTGCAAT TTAAGGATTG CGTCAGTCCG TGGCACHATAC TTTAGATTGT TACGCGAGTA GCAGTAGGAG CCGTGGCAGT
    ^-10 region of tet resistance promoter ^start of tet resistance translation
3201 CCCTGGATGC TGTAGGATA GGCTTGGTTA TGCCGGTACT GCCGGCCTC TTCCGGGATA TCGTCCATTC CGACAGCATC GCCAGTCACT ATGCCGTGCT
    GGGACCTACG ACATCCGTAT CCGAACCAAT ACGGCCATGA CCGCCGGAG AACGCCCTAT AGCAGGTAAG GCTGTGCTAG CCGTCAGTGA TACCGCACGA
3301
```

FIG. 16A

1 GAATTCAACT TCTCCATACT TTGGATAAGG AATACAGAC ATGAAAAATC TCATTGCTGA GTTGTATTAT AAGTTGCCC AAAAAGAAGA AGAGTCGAAT
CTTAAGTTGA AGAGGTATGA AACCTATCC TTTATGTCTG TACTTTTAG AGTAACGACT CAACAATAAA TTCGAACGGG TTTTCTTCT TCTCAGCTTA
101 GAACGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACACGG GTTGATTGAT CAGGTAGAGG
CTTGACACAC GCGTCCATCT TCGAAACCTC TAATAGCAGT GACGTTACGA AGGTTTATAC CGCGTTTATC TGGTTGTGCG CAACTAAC TA GTCCATCTCC
201 GGGCGCTGTA CGAGGTAAAG CCGCATGCCA GCATTCCTGA CGACATACG GAGCTGCTGC GCGATTAGCT AAAGAAATTA TTGAAGCATC CTGCTCAGTA
CCCGGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA TTTCTTCAAT AACCTCGTAG GAGCAGTCAT
301 AAAAGTTAAT CTTTCAACA GCTGTCAATA AGTTGTACG GCCGAGACT ATAGTCGCTT TGTTTTATT TTTTAATGTA TTGTAACTA GTACGCAAGT
TTTTCAATTA GAAAGTTGT CGACAGTATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA ACAAATAAA AAAATTACAT AAACATTGAT CATGCGTTCA
401 TCACGTAAAA AGGGTATCTA GAATTATGAA GAAGATATC GCATTTCTTC TTGCACTAT TTGCTTTT TCTATTGCTA CAAACGCGTA CGCTGATATC
AGTGCAATTT TCCCATAGAT CTTAATACTT CTTCCTATAG CGTAAAGAG AAGGTAGATA CAAGCAAAA AGATAACGAT GTTTGCGCAT GCGACTATAG
1 M K K N I A F L L A S M F V F S I A T N A Y A D I
Anti-VEGF Light chain (version Y0317)^
^STII Signal TIR -1
501 CAGTTGACCC AGTCCCGGAG CTCCTGTGCG GCATAGGCT CACCATCACC TGCAGCGCAA GTCAGATAT TAGCAACTAT TTAACCTGGT
GTCRACTGG TCAGGGGCTC GAGGACAGG CGGACACACC CGCTATCCCA GTGGTAGTGG ACGTCGCGTT CAGTCCTATA ATCGTTGATA AATTGACCA
26 Q L T Q S P S S L S A S V G D R V T I T C S A S Q D I S N Y L N W Y
601 ATCAACAGAA ACCAGGAAAA GCTCCGAAAG TACTGAATTA CTTCACCTCC TCTCTCACT CTGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC
TAGTTGTCTT TGGTCCTTTT CGAGGCTTTC ATGACTAAT GAAGTGGAGG AGAGAGTGA GACCTCAGG AAGACGGAAG AGACCTAGGC CAAGACCCTG
60 Q Q K P G K A P K V L I Y F T S S L H S G V P S R F S G S G S T
701 GGAATTCAC CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTGTCA ACAGTATAGC ACCGTGCCGT GGACGTTTGG ACAGGGTACC
CCTAAAGTGA GACTGGTAGT CGTCAGAGCT CGGTCTCTCTG AAGCGTTGAA TAATGACAGT TGTATATCG TGGCACGGCA CCTGCAAAACC TGTCCCATGG
93 D F T L T I S S L Q P E D F A T Y Y C Q Q Y S T V P W T F G Q G T
801 AAGTGGAGA TCAACGAAAC TGTGGCTGCA CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT GTGTGCCCTGC
TTCCACCTCT AGTTTGTCTG ACACCGAGCT GGTAGACAGA AGTAGAAGG CGGTAGACTA CTCGTCAACT TTAGACCTTG ACGAAGACAA CACACGGACG
126 K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V V C L L
901 TGAATAACTT CTATCCAGA GAGGCCAAAG TACAGTGGAA GGTGGATAAC GCCCTCCAAT CCGGTAACTC CCAGAGAGT GTCACAGAGC AGGACAGCAA
ACTTATTGAA GATAGGTCT CTCGGTTTC ATGTCACCTT CCACCTATTG CGGGAGTTA GCCCATCTCA CAGTGTCTCG TCCTGTCTGTT
160 N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K

FIG. 16B

1001 GGACAGACC TACAGCCTCA GCAGCACCT GACGTGAGC AAAGCAGACT ACAGAGAAACA CAAAGTCTAC GCCTCGAAG TCACCCATCA GGGCCTGAGC
CCTGTCGTGG ATGTCGGAGT CGTCGTGGGA CTGCGACTCG TTTCGTCTGA TGTCTTTGT GTTTCAGATG CGGACGCTTC AGTGGTAGT CCCGGACTCG
193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S
1101 TCGCCCGTCA CAAAGAGCTT CAACAGGGGA GAGTGTAAAT TAAATCCTCT AGCCGGAGC CATCGTGCG AGCTCGGTAC CCGGGATCT AGGCCTAACG
AGCGGGCACT GTTCTCGAA GTTGTCCTCT CTCACAATTA ATTTAGGAGA TCGCGCCTGC GTAGCACGC TCGAGCCATG GGCCCCCTAGA TCCGGATTGC
226 S P V T K S F N R G E C O
1201 CTCGGTTGCC GCGGGCGTT TTTTATTGTT GCCGACGCG ATCTCGAATG AACTGTGTGC GCAGGTAGAA GCITTTGGAGA TTATCGTCAC TGCAATAGCTT
GAGCCAACGG CCGCCCGCAA AAAATAACAA CCGCTGCGG TAGAGTTAC TTGACACACG CGTCCATCTT CGAAACCTCT AATAGCAGTG ACGTTACGAA
1301 CGCAATATGG CGCAAAATGA CCAACAGCG TTGATTGATC AGGTAGAGGG GCGGCTGTAC GAGTAAAGC CCGATGCCAG CATTCCTGAC GAGGATACGG
GCGTTATACC GCGTTTTACT GGTGTGCGC AACTAACTAG TCCATCTCC CCGGACATG CTCCATTTCC GGCTACGGTC GTAAGGACTG CTGCTATGCC
1401 AGCTGCTGCG CGATTACGTA AAGAAGTTAT TGAAGCATCC TCGTCAGTAA AAGTTAATC TTTTCAACAG CTGTCAATAA GTTGTACCG CCGAGACTTA
TCGACGACGC GCTAATGCAAT TTCTTCAATA ACTTCGTAGG AGCAGTCAIT TTTCATATAG AAAAGTTGTC GACAGTATTT CAACAGTGCC GGCTCTGAAT
1501 TAGTCGCTTT GTTTTATT TTTAATGAT TTGTAACCTAG TACGCAAGTT CACGTAAAAA GGATATCTAG AATTAGAAG AAGAATATCG CATTTCTTCT
ATCAGGAAA CAAAAATAAA AAATTACATA AACATTGATC ATGCGTTCAA GTGCATTTTT CCCATAGATC TTAATCTTC TTCTTATAGC GTAAAGRAGA
1 M K K N I A F L L
*STII Signal TIR-1
10 A S M F V F S I A T N A Y A E V Q L V E S G G L V Q P G G S L R
*Anti-VEGF Heavy Chain (version Y0317)
1701 TTGTCTGTG CAGCTTCTGG CTAGACTTC ACGCACTAG GTATGAATG GGTCCGTCAG GCCCCGGTA AGGGCTGGA ATGGGTGGA TGGATTAAACA
AACAGGACAC GTCGAAGACC GATGCTGAAG TCGCTGATGC CATCTTGAC CCAGGCAGTC CCGGGCCCAT TCCCGGACCT TACCCAACT ACCTAATGT
43 L S C A A S G Y D F T H Y G M N W V R Q A P G K G L E W V G W I N T
1801 CCTATACCG TGAACCGACC TATGCTGCG ATTTCAAAG TCGTTTCACT TTTTCTTTAG ACACCTCAA AAGCACAGCA TACCTGCAGA TGAACAGCCT
GGATATGCC ACTTGGCTGG ATACGACGCC TAAAGTTTGC AGCAAGTGA AAAAGAAATC TGTGAGGTT TCTGTCGTCT ATGGACGTCT ACTTGTGGA
77 Y T G E P T Y A A D F K R R F T F S L D T S K S T A Y L Q M N S L
1901 GCGCGCTGAG GACACTGCC TCTATTACTG TGCAAGTAT CCGTACTATT ATGGGACGAG CCACTGSTAT TTCGAGTCT GGGGTCAAGG AACCTGGTC
CGCGGACTC CTGTGACGGC AGATAATGAC ACGTTTCTAG GGCATGATA TACCCTGCTC GGTGACCATA AAGCTGCAGA CCCAGTCC TTGGGACCAG
110 R A E D T A V Y Y C A K Y P Y Y Y G T S H W Y F D V W G Q G T L V
2001 ACCGTCTCCT CCGCCTCCAC CAAGGGCCCA TCGTCTTCC CCTGSCACC CTCCTCCAAG AGCACTCTG GGGGCACAGC GGCCCTGGGC TGCTGTGTC
TGGCAGAGA GCGGAGGTG GTTCCCGGGT AGCCAGAAG GGGACGTGG GAGGAGTTC TCGTGGAGAC CCCCCTGTG CCGGGACCG ACGGACCACT
143 T V S S A S T K G P S V F P L A P S S K S T S G G T A A L G C L V K

FIG. 16C

2101 AGGACTACTT CCCGAAACG GTGACGGTGT GTTGAACCT AGGGGCCCTG ACCAGCGCGT TGACACACTT CCGGCTGTCT CTACAGTCTT CAGGACTCTA
TCCTGTGAA GGGCTTGGC CACTGCGACA GCACCTTGAG TCCGCGGC AGTGTGGA AGTGTGGA GATGTGAGGAT GTCTGTGAT
177 D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S G L Y
2201 CTCCTCAGC AGCGTGTGA CTGTGCCCTC TAGCAGCTTG GGCACCGA CTTACATCTG CAACGTGAAT CACAGCCCA GCAACACCA GGTGACAAAG
GAGGAGTGTG TCGACCACT GACACGGAG ATCGTGAAC CCGTGGGTCT GATGTGAGC GTTGTGAGT GTTGTGAGT CCGCTGTG
210 S L S S V V T V P S S S L G T Q T Y I C N V N H K P S N T K V D K
2301 AAAGTTGAGC CCAATCTTG TGACAAACT CACACATGCC CACGTGCCC AGCACCTGAA CTCTGGGG GACCGTCACT TTCTCTCTT CCCCCAAAC
TTTCACTG GGTGAGAC ACTGTTTGA GTGTGTAGG GTGACCGG GTGACCGG TCGTGACTT GAGGACCCCT CTGGCAGTCA GAGGAGAG GGGGTTTG
243 K V E P K S C D K T H T C P P C P A P E L L G G P S V F L F P P K P
2401 CCAAGGACAC CTTATGATC TCCCGACCC CTGAGGTAC ATGCGTGGT GTGACGTGA GCGACGAGA CCTGTAGGTC AAGTTCACT GGTACGTGGA
GGTTCTGTG GAGTACTAG AGGCGCTGG GACTCCAGT TACGACAC CACTGCACT CGGTGCTTCT GGGACTCCAG TTCAAGTTGA CCAATGCACT
277 K D T L M I S R T P E V T C V V V D V S H E D P E V K F N W Y V D
2501 CGCGTGGAG GTGCATAATG CCAAGACAAA GCGCGGGAG GAGCAGTACA ACAGACGTA CCGTGTGCTC AGCTCTCTCA CCGTCTTGA CCAGGACTGG
GCCGACCTC CACGTATTAC GGTCTGTGTT CCGCGCCCTC CTGCTCATGT TGTGTGATGT GGCACACAG TCGCAGGAGT GGCAGGAGT GGTCTGTACC
310 G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H Q D W
2601 CTGAATGCA AGGAGTACAA GTGCAAGTCT TCCAACAAAG CCCTCCAGC CCGCATCGAG AAAACCATCT CCAAGGCCAA AGGGCAGCCC CGAGAACCA
GACTTACCTT TCCTCATGTT CACGTTCAG AGTTGTTTC GGGAGGCTG GGGTAGTCT TTTTGTGTA GGTTCGCTT TCCGCTGGG GCTCTTGTG
343 L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R E P Q
2701 AGGTGTACAC CTTGCCCTCA TCCCGGAG AGATGACCAA GACAGGTC AGCTGACCT GCCTGGTCAA AGCTTCTAT CCAGCGACA TCGCGGTGGA
TCCACATGTG GAGCGGGT AGGGCCCTTC TCTACTGTTT CTGTGTCCAG TCGGACTGGA CCGACCACTT TCCGAAGATA GGTGTGCTGT AGCGGACCT
377 V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I A V E
2801 GTGGGAGAGC AATGGCAGC CGGAGAACA CTACAGACC AGCGCTCCG TGCTGACTC CGAGGCTCC TTCTTCTCT ACAGCAAGT CACCGTGGAC
CACCTCTG TTACCGGTG GCCTCTGTT GATGTTCTG GTGAGGCG GCTGCCGAG AGAAGAGA TGTGTGGA GTGCGACCTG
410 W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L T V D
2901 AAGAGCAGT GGCAGCAGG GAAGTCTTC TCATGCTCG TGATGCTGA GGTCTGAC AACACTACA CCGAGAGAG CCTCTCCCTG TCTCGGGTA
TTCTCGTCCA CCGTGTCTCC CTTCAGAG AGTACAGGC ACTAGTACT CCGAGAGTG TTGTGATGT GGTCTCTC GAGAGGAG AGAGGCCAT
443 K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S P G K
3001 AATAGCATG CGAGCGCCT AGAGTCCCTA AGCTCGGT GCGCGCGGC GTTTTATT GTTAACAT GTTGACAGC TTATCATGA TAAGCTTTAA
TTATGTGAT GCTGCGGGA TCTCAGGAT TCGAGCCAA CCGCGGCGCG CAATAATAA CAATTGAGTA CAACTGTG AATAGTAGT ATTGAAAT
477 O
3101 TCGGTAGT TATCAGAT AAATTGCTAA CCGAGTCAAG CACGTGTAT GAAATCTAAC AATGGCTCA TGTCTATCT CGGCAACGTC ACCCTGGAT
AGCCATCAA ATAGTGTCAA TTAAAGATT GGTCACTCC GTGGACATA CTTTAGATT TTACGAGT AGCAGTAGA GCGGTGGCAG TGGGACCTAC
*Start Tet Resistance Coding Sequence

FIG. 16D

3201 CTGTAGGCAT AGGCTTGTT ATGCCGGTAC TGCCGGGCT CTTGGGGAT ATCGTCCATT CCGACAGCAT CGCCAGTCAC TATGGCGTGC TGCTAGCGCT
GACATCCGTA TCCGAACCAA TAGGGCCATG ACGGCCCCGA GAACGCCCTA TAGCAGGTAA GGCTGTCGTA GCGGTCAGTG ATACCCACG ACGATCGGGA

3301

FIG. 17A

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1 GAATTCAACT TCTCCATACT TTGGATAAGG AATACAGAC ATGAAAAATC TCATTGCTGA GTTGTATTTT AAGCTTGCCC AAAAAAGA AGATCGAAT
  CTTAAGTTGA AGAGGTATGA AACCTATTCC TTTATGCTG TACTTTTAG AGTAACGACT CAACAATAA TTCGAACGGG TTTTCTTCT TCTCAGCTTA

101 GAACTGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATGCT TGGCAATATG GCGCAAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAGG
  CTTGACACAC GCGTCCATCT TCGAAACCTC TAATAGCAGT GACGTACGA AGGTTATAC CGGTTTTTAC TGGTTGTGCG CAACTAACTA GTCCATCTCC

201 GGGCGCTGTA CGAGGTAAG CCGATGCCA GCATTCCCTGA CGACATAGC GAGCTGCTGC GCGATTACGT AAAGAAGTTA TTGAAGCATC CTCGTCACTA
  CCCGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GCTGATGCT GCTGACGACG CGCTAATGCA TTTCTTCAAT AACTTCGTAG GACGAGTCAT

301 AAAAGTTAAT CTTTCAACA GCTGTCAATA AGTTGTCAGG GCCGAGACTT ATAGTCGCTT TGTGTTTAT TTTTAAATGA TTTGTAACCTA GTACGCAAGT
  TTTTCAATTA GAAAGTTGT CGACAGTATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA ACAAAATAA AAAATTACAT AAACATTGAT CATGCGTTCA

401 TCAGGTAAA AGGTATCTA GAATTATGAA GAAGATATC GCATTCTTTC TTGCACTAT TTGCGTTTTT TCTATTGCTA CAAACGCGTA CGCTGATATC
  AGTGCATTTT TCCCATAGAT CTTAATACTT CTTCCTATAG CGTAAAGAAG AAGCTAGATA CAAGCAAAA AGATAACGAT GTTTGGCAT GCGACTATAG
  1 M K K I A F L L A S M F V F S I A T N A Y A D I
    ^STII Signal TIR -1
    ^anti-VEGF Light Chain^

501 CAGTTGACCC AGTCCCGGAG CTCCTGTGCC GCCTCTGTGG GCGATAGGGT CACCATCACC TGCAGCGCAA GTCAGGATAT TAGCAACTAT TTAAACTGGT
  GTCACTGGG TCAGGGGCTC GAGGGACAGG CGGACACACC CGCTATCCCA GTGGTAGTGG ACGTCGCGTT CAGTCCTATA ATCGTTGATA AATTGACCA
  26 Q L T Q S P S S L S A S V G D R V T I T C S A S Q D I S N Y L N W Y
    ^variable light (VL) cys

601 ATCAACAGAA ACCAGGAAA GCTCCGAAAG TACTGATTTA CTTACCTCC TCTCTCCACT CTGAGTCCC TTCTCGCTTC TCTGATCCG GTTCTGGGAC
  TAGTTGTCTT TGGTCCCTTT CGAGGCTTTC ATGACTAAT ATGACTAAT GAAGTGGAGG AGAGAGTGA GACCTCAGG AAGAGCGAAG AGACCTAGGC CAAGACCCCTG
  60 Q Q K P G K A P K V L I Y F T S S L H S G V P S R F S G S G S G T

701 GGATTTCACT CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTCTCA ACAGTATAGC ACCGTGCCGT GGACGTTTGG ACAGGGTACC
  CCTAAAGTGA GACTGGTAGT CGTCAGAGGT CGGTCTTCTG AAGCGTTGAA TAATGACAGT TGTATATCG TGGCAGCGCA CCTGCAACC TGTCCTCATGG
  93 D F T L T I S S L Q P E D F A T Y Y C Q Q Y S T V P W T F G Q G T
    ^Variable light cys

801 AAGTGGAGA TCAACGAAC TGTGGTGCA CCACTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TCGTCTCTGT GTGTGCCCTG
  TTCCACCTCT AGTTTGCTTG ACACCGAGGT GGTAGACAGA AGTAGAAGG CGGTAGACTA CTCGTCAACT TTAGACCTTG ACGAAGACAA CACACGACG
  126 K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V V C L L
    Constant Light cys^
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FIG. 17B

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901 TGAATAACTT CTATCCCGA GAGGCCAAG TACAGTGAA GGTGATAAC GCCTCCCAAT CGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA
    ACTTATTGAA GATAGGGTCT CTCGGGTTTC ATGTCACCTT CCACCTATTG CGGAGAGTTA GCCCATAGAG GGTCTCTTCA CAGTGTCTCG TCCTGTCTGT
160 N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K

1001 GGACAGACC TACAGCCTCA GCAGCACCTT GAGCTGAGC AAAGAGACT ACGAGAACA CAAAGTCTAC GCTGCGAAG TCACCCATCA GGGCCTGAGC
    CCTGCTGG ATGTCGGAGT CGTCGTGGGA CTGGGACTCG TTTCGTCTGA TGCTCTTTGT GTTTCAGATG CGGACGCTTC AGTGGTAGT CCCGACTCG
193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S
    ^Constant Light cys

1101 TCGCCCGTCA CAAAGAGCTT CAACAGGGA GAGTGTTAAT TAAATCCTCT ACGCCGGAGC CATCGTGGCG AGCTCGGTAC CCGGGGATCT AGGCCTAAGC
    AGCGGCGAGT GTTCTCGAA GTTGTCCTCT CTCACAATTA ATTTAGGAGA TCGCGCCTGC GTAGCACCGC TCAGAGCCATG GGCCCTTAGA TCCGGATTGC
226 S P V T K S F N R G E C O
    ^cys to bind heavy
    start lambda to terminator^

1201 CTCGGTTGCC GCGGGGCGTT TTTTATTGTT GCGGACGCGC ATCTCGAATG AACTGTGTGC GCAGGTAGAA GCTTTGGAGA TTATCGTCAC TGCAATGCTT
    GAGCCAACGG CGGCCCGCAA AAAATAACAA CGGCTGCGG TAGAGCTTAC TTGACACACG GGTCCATCTT CGAAACCTCT AATAGCAGTG ACGTTACGAA
    ^end lambda to terminator

1301 CGCAATATGG CGCAAAATGA CCAACAGCGG TTGATTGATC AGGTAGAGGG GGCCTGTGAC GAGGTAAGC CCATGTCAG CATTCTGAC GACGATACGG
    GCGTTATACC GCGTTTACT GGTGTGCGC AACTAATAG TCCATCTCCC CCGGACATG CTCATTTTCG GGCTACGGTC GTAAGGACTG CTGCTATGCC

1401 AGCTGTGCG CGATTACGTA AAGAAGTAT TGAAGCATCC TCGTCAGTAA AAGTTAATC TTTCACACG CTGTCAATAA GTTGTACCG CCGAGACTTA
    TCGACGACGC GCTAATGCAAT TTCTTCAATA ACTTCGTAGG AGCAGTCATT TTTCATTTAG AAAGTTGTC GACAGTATTT CAACAGTGCC GGCTCTGAAT

1501 TAGTCGCTTT GTTTTATT TTGAATGAT TTGPAACTAG TACGCAAGTT CACGTAATAA GGGTATCTAG AATPATGAG AAGAATATCG CATTTCTTCT
    ATCAGCGAAA CAAAAATAA AAATTACATA AACATTGATC ATGCGTTCAA GTGCATTTT CCCATAGATC TTAATACTTC TTCTTATAGC GTAAAGAAGA
    M K K N I A F L L
    ^STII Signal TIR-1

1601 TGCATCTATG TTCGTTTTT CTATTGCTAC AAACGCGTAC GCTCAGGTTC AGCTGGTGA GTCTGGCGCA GAGGTGAAA AGCCAGGGGC TTCAGTTAAA
    ACGTAGATAC AAGCAAAAAA GATAACGATG TTTTCGCGATG CGAGTCCAAG TCGACCAAGT CAGACGCGT CTCACATTTT TCGGTCCCCG AAGTCAATTT
10 A S M F V F S I A T N A Y A Q V Q L V Q S G A E V K K P G A S V K
    ^anti-VEGF Heavy Chain (VNERK version)
    ^Heavy Chain FR1 changed to SubgroupI consensus sequence

1701 GTATCTCTGA AAGCTTCTGG CTATACCTTC ACCAACTATG GTATAACTG GGTCCGTGAG GCCCGGGTA AGGSCCTGGA ATGGGTGGA TGGATTAAAC
    CATAGGACAT TTCGAAGACC GATATGGAAG TGTTGTATAC CATATTGAC CCAGCGAGTC CGGGGCCAT TCCCGGACT TACCCAACT ACCTAATTTG
43 V S C K A S G Y T F T N Y G I N W V R Q A P G K G L E W V G W I N T
    ^Variable Heavy (VH) cys

1801 CCTATACCGG TGAACCGACC TATGTGCGG ATTTCAACG TCGTTTCACT TTTTCTTTAG ACACCTCCAA AAGCACAGCA TACCTGCAGA TGAACAGCCT
    GGATATGCC ACTTGGCTGG ATACGACGCC TAAAGTTTGC AGCAAAATGA AAAAGAAATC TGTGGAGTT TCTGTCTGT ATGGACGTCT ACTTGTGCGA
77 Y T G E P T Y A A D F K R R F T F S L D T S K S T A Y L Q M N S L

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FIG. 17C

1901 GCGCGCTGAG GACACTGCCG TCTATTACTG TGCAGAGTAC CCGCACTATT ATGTGAACGA GCGGAAGAGC CACTGGTATT TCGACGTCTG GGTCAAGGA
CGCGGCACTC CTGTGACGGC AGATAATGAC ACGTTTCATG GCGGTGATAA TACACTTGCT CGCTTCTCG GTGACCATAA AGCTGCAGAC CCCAGTTCCT
110 R A E D T A V Y Y C A K Y P H Y Y V N E R K S H W Y F D V W G Q G
^VH cys
2001 ACCCTGGTCA CCGTCTCCTC GGCTCCACC AAGGCCCAT CCGTCTTCCC CTGGCACCC TCCTCCAAGA GCACCTCTGG GGGCACAGCG GCCTGGGCT
TGGGACCACT GGCAGAGGAG CCGGAGGTGG TTCCCGGGTA GCCAGAAGG GACCCGTGG AGAGGTCT CGTGGAGACC CCGGTGTGCG CGGACCCGGA
143 T L V T V S S A S T K G P S V F P L A P S S K S T S G G T A A L G C
Constant Heavy 1 (CH1) cys^
2101 GCCTGGTCAA GGACTACTTC CCGAACCGG TGACGGTCTC GTGAACTCA GCGGCCCTGA CAGCGGGGT GCACACCTTC CCGGCTGTCC TACAGTCTTC
CGGACCACTT CCTGATGAAG GGGCTTGCC ACTGCCACAG CACCTTGAGT CCGCGGACT GGTGCGCA CGTGTGGAAG GCGCGACAG ATGTGAGGAG
177 L V K D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S
2201 AGGACTCTAC TCCCTCAGCA GCGTGTGAC TGTGCCCTCT AGCAGTTGG GCACCCAGAC CTACATCTGC AACGTGAATC ACAAGCCCAG CAACACCAAG
TCCTGAGATG AGGGATCGT CGCACCACTG ACACGGGAGA TCGTGAACC CGTGGGTCTG GATGTAGACG TTGCACTTAG TGTTCGGTC GTTCTGGTTC
210 G L Y S L S S V V T V P S S L G T Q T Y I C N V N H K P S N T K
^CH1 cys
2301 GTGGACAAGA AAGTTGAGCC CAAATCTTGT GACAAAACCT ACACATGCCC ACCGTGCCA GCACCTGAAC TCCTGGGGG ACCGTGAGTC TTCTCTTCTC
CACCTGTTCT TTCAACTCGG GTTTAGAACA CTGTTTGTAG TGTGTACGG TGGCAGGGT GGTGACTTG AGGACCCCCC TGGCAGTCAG AAGGAGAAGG
243 V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F L F P
^cys to bind light chain ^hinge cys
2401 CCCCCAAACC CAAGACACC CTCATGATCT CCGGACCCC TGAGTCACTA TCGTGTGTGG TGGACGTGAG CCACGAAGAC CCGTGGTCA AGTTCAACTG
GGGGTTTTGG GTTCCTGTGG GAGTACTAGA GGGCTGGGG ACTCCAGTGT ACCACACCACC ACCTGCACTC GGTGCTTCTG GGACTCCAGT TCAAGTTGAC
277 P K P K D T L M I S R T P E V T C V V V D V S H E D P E V K F N W
^Constant Heavy 2 (CH2) cys
2501 GTACGTGGAC GGGGTGGAGG TGCATAATGC CAAGACAAG CCGCGGGAGG AGCAGTACAA CAGCACGTAC CGTGTGGTCA GGTCTCTCAC CGTCTGCAC
CATGCACCTG CCGCACCTCC ACGTATTACG GTTCTGTTTC GCGGCCCTCC TCGTCATGTT GTCTGTGATG GCACACCACT CCGCAGGAGTG GCAGGACGTG
310 Y V D G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H
2601 CAGGACTGGC TGAATGGCAA GGAGTACAG TGCAGGTCT CCAACAAGC CCTCCAGCC CCCATCGAGA AAACCATCTC CAAAGCCAAA GGGCAGCCCC
GTCTGACCG ACTTACCGTT CCTCATGTT CCGTCCAGA GGTGTTTCG GGAGGGTCTG GGTGAGTCTT TTTGTAGAG GTTTCGGTTT CCGCTCGGG
343 Q D W L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R
^CH2 cys
2701 GAGAACCA GGTGTACACC CTGCCCCCAT CCGGGGAAGA GATGACCAAG AACAGGTCA GCCTGACCTG CCTGGTCAA GGTCTCTATC CCAGCGACAT
CTCTTGGTGT CCACATGTGG GACGGGGTA GGGCCCTTCT CTACTGTTTC TTGTTCCAGT CCGACTGGAC GGACCACTTT CCGAAGATAG GGTCTGCTGA
377 E P Q V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I
^Constant Heavy 3 (CH3) cys

FIG. 17D

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2801 CGCGTGGAG TGGGAGGCA ATGGGAGCC GGAGAACAAAC TACAAGACCA CGCTCCCGT GCTGGACTCC GACGGCTCCT TCTTCTCTTA CAGCAAGCTC
CGGCACCTTC ACCCTCTCGT TACCGGTCCG CCTCTTGTG ATGTTCTGGT GGGAGGGCA CGACCTGAGG CTGCCGAGGA AGAAGGAGAT GTCGTTGAG
410 A V E W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L
2901 ACCGTGGACA AGAGCAGGTG GCAGCAGGGG AACGTCTTCT CATGCTCCGT GATGCATGAG GCTCTGCACA ACCACTACAC GCAGAAGAGC CTCTCCCTGT
TGGCACCTGT TCTCGTCCAC CGTCGTCCCG CTGCAGAGA GTACGAGGCA CTACGTACTC CGAGACGTGT TGGTGATGTG CGTCTTCTCG GAGAGGGACA
443 T V D K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S
^CH3 cys
3001 CTCGGGTAA ATAAGCATGC GACGGCCCTA GAGTCCCTAA CGCTCGGTG CCGCCGGGGC TTTTATTG TTAATCATG TTTGACAGCT TATCATCGAT
GAGGCCCAT TATTCGTACG CTGCCGGGAT CTCAGGGATT GCGAGCCAAC GGGGGCCCGC AAAAAATAAC AATTGAGTAC AACTGTGCA ATAGTAGCTA
477 P G K O
^start lambda t0 terminator ^end lambda t0 terminator
^start of tet resistance promoter ^-35 of promoter
3101 AAGCTTAAAT GCGGTAGTTT ATCACAGTTA AATTGCTAAC GCAGTCAGGC ACCGTGTATG AAATCTAACA ATGCCGTCAT CGTCATCCTC GGCACCGTCA
TTCGAAATTA CGCCATCAAA TAGTGTCAT TTAAGGATTG CGTCAGTCCG TGSCACATAC TTTAGATTGT TACGGAGTA GCAGTAGGAG CCGTGGCAGT
^-10 region of tet resistance promoter ^start of tet resistance translation
3201 CCCTGGATGC TGTAGGATA GGCTTGGTTA TGCCGGTACT GCCGGCCTC TTGCGGGATA TCGTCCATTC CGACAGCATC GCCAGTCACT ATGGCGTGCT
GGGACCTACG ACATCCGTAT CCGAACCAAT ACGGCCATGA CCGCCCGGAG AAGCCCTAT AGCAGGTAAG GCTGTCGTAG CGGTCACTGA TACCGCACGA
3301

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FIG. 18A

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1  GAATTCAACT TCTCCATACT TTGATAAGG AATACAGAC ATGAAAATC TCATTGCTGA GTTGTTATTT AAGCTTGCCC AAAAAGAAGA AGAGTCGAAT
   CTTAAGTTGA AGAGGTATGA AACCTAITCC TTTATGCTG TACTTTTAG AGTAACGACT CAACAATAAA TTCGAACGGG TTTTCTTCT TCTCAGCTTA

101  GAACGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAGG
   CTTGACACAC GCGTCCATCT TCGAAACCTC TAATAGCAGT GACGTTACGA AGCGTTATAC CGCGTTTAC TGGTTGTGCG CAACTAACATA GTCCATCTCC

201  GGGCGCTGTA CGAGGTAAAG CCGATGCCA GCATTCCTGA CGACGATACG GAGCTGCTGC GCGATTACGT AAAGAAGTTA TTGAAGCATC CTCGTCAGTA
   CCCGCGACAT GCTCCATTTC GGGTACGGT CGTAAGGACT GCTGTATGC CTCGACGACG CGCTAATGCA TTTCTTCAAT AACTTCGTAG GAGCAGTCAT

301  AAAAGTTAAT CTTTCAACA GCTGTCAATA AGTTGTCACG GCGGAGACTT AVAGTCGCTT TGTITTTTAT TTTTAATGTA TTGTAACTA GTACGCAAGT
   TTTTCAATTA GAAAAGTTGT CGACAGTATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA ACAAAATAA AAAATTACAT AAACATTGAT CATCGGTTCA

401  TCACGTAAAA AGGTATCTTA GAATTATGAA GAAGAATATC GCATTTCTTC TTGCATCTAT GTTCGTTTTT TCTATTGCTA CAAACGCGTA CGTGTATATC
   AGTGCAATTT TCCCATAGAT CTTAATACTT CTTCTTATAG CGTAAGAAG AACGTAGATA CAAGCAAAA AGATAACGAT GTTTGCGCAT CGGACTATAG
   1      M K K N I A F L L A S M F V F S I A T N A Y A D I
           ^STII Signal TIR -1                                anti-VEGF Light Chain^

501  CAGTTGACCC AGTCCCGAG CTCCTGTCC GCCTCTGTG GCGATAGGT CACCATCAC TGCAGCGCAA GTCAGGATAT TAGCAACTAT TTAACCTGGT
   GTCAACTGGG TCAGGGGCTC GAGGGACAGG CGGACACACC CGCTATCCCA GTGGTAGTGG ACGTGGCGTT CAGTCTCTATA ATCGTTGATA AATTGACCA

26 Q L T Q S P S S L S A S V G D R V T I T C S A S Q D I S N Y L N W Y
   ^variable light (VL) cys

601  ATCAACAGAA ACCAGGAAA GCTCCGAAAG TACTGATTTA CTTCACTCC TCCTCTCCACT CTGGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC
   TAGTTGTCTT TGGTCCCTTT CGAGGCTTTC ATGACTAAT GAAGTGGAGG AGAGAGGTGA GACCTCAGG AAGAGCGAAG AGACCTAGGC CAAGACCCCTG

60 Q Q K P G K A P K V L I Y F T S S L H S G V P S R F S G S G T
   ^variable light cys

701  GGATTTCACT CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTGTCA ACAGTATAGC ACCGTGCCGT GGACGTTTGG ACAGGGTACC
   CCTAAGTGA GACTGGTAGT CGTCAGACGT CGGTCTTCTG AAGCGTTGAA TAATGACAGT TGTATATCG TGGCAGGGCA CCTGCAAACC TGTCCCATGG

93 D F T L T I S S L Q P E D F A T Y Y C Q Q Y S T V P W T F G Q G T
   ^variable light cys

801  AAGGTGGAGA TCAACGAAC TGTGGGTGCA CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT GTGTGCTGTC
   TTCCACCTCT AGTTTGCTTG ACACCGACGT GGTAGACAGA AGTAGAGGG CGGTAGACTA CTCGTCAACT TTAGACCTTG ACGAAGACAA CACACGGAGC

126 K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V V C L L
   Constant Light cys^
```

FIG. 18B

901 TGAATAACTT CTATCCAGA GAGGCCAAG TACAGTGAA GGTGGATAAC GCCCTCCAAT CGGTAACCTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA
ACTTATTGAA GATAGGGTCT CTCGGGTTTC ATGTCACCTT CCACCTATTG CCGGAGGTGA GCCATTGAG GGTCCTCTCA CAGTGTCTCG TCCTGTCTGT
160 N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K
1001 GGACAGACC TACAGCCTCA GCAGCACCTT GACCTGAGC AAAGCAGACT ACAGAAAACA CAAAGTCTAC GCCTGCGAAG TCACCCATCA GGGCCTGAGC
CCTGCTGAG ATGTCGGAGT CGTCGGTGGG CTGCGACTCG TTTCGCTGTA TGCTCTTTGT GTTTCAGATG CGGAGCTTC AGTGGGTAGT CCGGAGTAGC
193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S
^Constant Light cys
1101 TCGCCCGTCA CAAAGAGCTT CAACAGGGGA GAGTGTAAAT TAAATCCTCT ACGCCGGAGC CATCGTGGCG AGCTCGGTAC CCGGGGATCT AGGCCTAACG
AGCGGGCAGT GTTCTCGAA GTTGTCCTCT CTCACAATTA ATTTAGGAGA TCGCGGCTGC GTAGCACCGC TCGAGCCATG GCGCCCTAGA TCGGATGTC
226 S P V T K S F N R G E C O
^cys to bind heavy start lambda t0 terminator^
1201 TCGGTGCGC GCGGGCGTT TTTTATTGTT GCCGAGCGC ATCTGAAATG AACTGTGTGC GCAGGTAGAA GCTTTGGAGA TTATCGTCAC TGCAATGCTT
GAGCAACGG CGGCCGCAA AAAATAACAA CCGCTGCGG TAGAGTTTAC TTGACACAGC CGTCCATCTT CGAAACCTCT AATAGCAGTG ACGTTACGAA
^end lambda t0 terminator
1301 CGCAATATGG CGCAAAATGA CCAACAGCGG TTGATTGATC AGGTAGAGG GCGGCTGTAC GAGTAAAGC CCGATGCCAG CATTCCTGAC GACGATACGG
CGGTTATACC GGGTTTACT GGTGTGCGC AACTAACTAG TCCATCTCC CCGCGACATG CTCCATTTCC GGCTACGGTC GTAAAGGACTG CTGCTATGCC
1401 AGCTGCTGG CGATTAGGTA AAGAAGTTAT TGAAGCATCC TCGTCAGTAA AAGTTAATC TTTTCAACAG CTGTCTATAA GTTGTACAGG CCGAGACTTA
TCGAGCAGC GCTAATGCA TTTCTCAATA ACTTCGTAGG AGCAGTCAIT TTTCAATTAG AAAAGTTGTC GACAGTATTT CAACAGTGCC GGCTCTGAAT
1501 TAGTCGCTTT GTTTTATTTT TTGTAAGTAT TTGTAAGTAT TACGCAAGTT CAGTAAAAA GGGTATCTAG AATTATGAG AAGAATATCG CATTTCTTCT
ATCAGCGAAA CAAAATATAA AAATTACATA AACATTGATC ATGCGTTCAA GTGCAITTTT CCATAGATC TTAATPACTTC TTCTTATAGC GTAAAGAAGA
M K K N I A F L L
^STII Signal TIR-1
1601 TGCATCTATG TTCGTTTTTT CTATTGCTAC AAACGCTAC GCTCAGTTTC AGCTGCAAGA GTCTGGCCCG GGCCTGGTGA AACCATCTCA GACTCTCTCC
ACGTAGATAC AAGCAAAAA GATAACGATG TTTGGCGATG CGAGTCCAAG TCGACGTTCT CAGACCGGCC CCGGACCACT TTGGTAGAGT CTGAGAGAGG
10 A S M F V F S I A T N A Y A Q V Q L Q E S G P G L V K P S Q T L S
^anti-VEGF heavy chain (VNERK version)
^Heavy chain FR1 changed to Subgroup II consensus sequence
1701 TTGACTTGTA CTGTTTCTGG CTATACCTTC ACCAACTATG GPATAACTG GGTCCGTCAG GCCCGGGGTA AGGGCTGGA ATGGGTTGGA TGGATTAAACA
AACTGAACAT GACAAAGACC GATATGGAAG TGGTTGATAC CATATTGAC CCAGGCGATC CCGGGCCCAT TCCCGGACCT TACCCAACT ACCTAATGT
43 L T C T V S G Y T F T N Y G I N W V R Q A P G K G L E W V G W I N T
^Variable Heavy (VH) cys
1801 CCTATACCG TGAACCGACC TATGCTGGG ATTTCAAAGC TGTTCACCT TTTTCTTTAG ACACCTCAA AAGCAGAGA TACCTGCAGA TGAACAGCCT
GGATATGCC ACTTGGCTGG ATACGAGGCC TAAAGTTTGC AGCAAGTGA AAAAGAAATC TGTGAGGT TTCTGTCTGT ATGGAGCTCT ACTTGTGGA
77 Y T G E P T Y A A D F K R R F T F S L D T S K S T A Y L Q M N S L

FIG. 18C

1901 GCGCGCTGAG GACACTGCCG TCTATTACTG TGCAAAAGTAC CCGCACTATT ATGTGAACGA GCGAAGAGC CACTGTGATT TCGACGTCTG GGTCAAGGA
CGCGGACTC CTGTGACGGC AGATAATGAC ACGTTTTCATG GCGGTGATAA TACACTTGCT CGCTTCTCG GTGACATATA AGCTGCAGAC CCCAGTTCCT
110 R A E D T A V Y Y C A K Y P H Y Y V N E R K S H W Y F D V W G Q G
^VH cys
2001 ACCCTGGTCA CGCTCTCCTC GGCTCCACC AAGGGCCCAT CGGTCTTCCC CTTGGCACCC TCCTCCAAGA GCACCTTGG GGGCACAGCG GCCTGGGCT
TGGACCACT GGCAGAGGAG CCGAGGTGG TTCCGGGTA GCCAAGGG GGACCGTGG AGAGGTCT CGTGAGACC CCCGTGTGCG CGGACCCGA
143 T L V T V S S A S T K G P S V F P L A P S S K S T S G G T A A L G C
Constant Heavy 1 (CH1) cys
2101 GCCTGGTCAA GGACTIONC CCGAACCGG TGACGGTCTC GTGGACTIONC GGGCCCTGA CCAGCGCGT GCACACTTC CGGCTGTCC TACAGTCTC
CGGACCACT CCTGATGAG GGGCTTGCC ACTGCCACAG CACTTGAGT CCGCGGACT GGTGCGGCA CGTGTGAG GCGCGACAGG ATGTCAAGG
177 L V K D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S
2201 AGGACTCTAC TCCCTCAGCA GCGTGTGAC TGTGCCCTCT AGCAGTTGG GCACCCAGAG CTACATCTGC AACGTGAATC ACAAGCCAG CAACACCAAG
TCCTGAGATG AGGAGTCGT CGCACCACTG ACACGGGAGA TCGTGAACC CGTGGTCTG GATGTAGACG TTGCACTTAG TGTTCGGTC GTTGTGTTT
210 G L Y S L S S V V T V P S S L G T Q T Y I C N V N H K P S N T K
^CH1 cys
2301 GTGGACAAGA AAGTTGAGCC CAAATCTGT GACAAACTC ACACATGCC ACCGTGCCA GCACCTGAAC TCCTGGGGG ACCGTGAGT TTCTCTTCC
CACCTGTTCT TTCAACTCGG GTTTAGAACA CTGTTTGGAG TGTGTACGG TGGACCGGT CGTGACTTG AGGACCCCGG TGGCAGTCAG AAGGAGAAG
243 V D K K V E P K S C D K T H T C P C P A P E L L G G P S V F L F P
^cys to bind light chain ^hinge cys
2401 CCCCACCAACC CAAGGACACC CTCATGATCT CCGGACCCC TGAGTCACTA TCGTGTGTGG TGGACGTGAG CCACGAAGAC CCTGAGTCA AGTTCAACTG
GGGGTTTGG GTTCCTGTGG GAGTACTAGA GGGCGTGGG ACTCCAGTGT C V V V D V S H E D P E V K F N W
277 P K P K D T L M I S R T P E V T
^Constant Heavy 2 (CH2) cys
2501 GTACGTGGAC GCGTGGAGG TGCAATATGC CAAGACAAG CCGCGGAGG AGCAGTACAA CAGCAGTAC CAGCAGTAC GGTGTGTCA GGTCTCTCAC CGTCTGAC
CATGACCTG CCGCACCTCC ACGTATTACG GTTCTGTTTC GCGCCCTCC TCGTCATGTT GTCTGTGATG GCACACCATG CGCAGGAGTG GCAGGACGTG
310 Y V D G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H
2601 CAGGACTGCG TGAATGGCAA GGAGTACAA GGTAGGTCT CCAACAAAG CCTCCAGCC CCATCGAGA AAACCATCTC CAAGGCCAA GGGCAGCCCC
GTCTGACCG ACTTACGTT CCTCATGTT CAGTTTCCAGA GGTGTGTTG GGAGGTGCG GGTGAGTCT TTTGTAGAG GTTTCGTTT CCCTCGGG
343 Q D W L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R
^CH2 cys
2701 GAGAACCA GGTGTACACC CTGCCCCCAT CCGGGAAGA GATGACCAAG AACAGGTCA GCCTGACCTG CCTGTCAA GGTCTCTATC CCAGCGACAT
CTCTTGGTGT CCACATGTGG GACGGGGTA GGGCCCTTCT CTACTGTTT TTTGTCTCAGT CCGACTGAC GACCACTTT CCGAAGATAG GGTCTGCTGA
377 E P Q V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I
^Constant Heavy 3 (CH3) cys

FIG. 18D

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2801 CGCCGTGGAG TGGGAGAGCA ATGGGCAGCC GGAGAACAAAC TACAAGACCA CGCTCCCGT GCTGGACTCC GACGGCTCCT TCTTCTCTTA CAGCAAGCTC
GGGCACCTTC ACCCTCTCGT TACCCGTGGG CCTCTGTGTG ATGTTCTGGT GCGGAGGCA CGACTGAGG CTGCCGAGGA AGAAGGAGAT GTGTTTCGAG
410 A V E W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L
2901 ACCGTGGACA AGAGCAGGTG GCAGCAGGGG AACGTCTTCT CATGCTCCGT GATGCATGAG GCTCTGCACA ACCACTACAC GCAGAAGAGC CTCTCCCTGT
TGGCACCTGT TCTCGTCCAC CGTCGTCCCC TTGCAGAAGA GTACGACTC CTACGACTC CGAGACGTGT TGGTATGTG CGTCTTCTCG GAGAGGGACA
443 T V D K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S
^CH3 cys
3001 CTCGGGTAA ATAAGCATGC GACGGCCCTA GAGTCCCTAA CGCTCGGTTG CGCCCGGGCG TTTTATTG TTAATCTATG TTGACAGCT TATCATCGAT
GAGGCCATT TATTCGTACG CTGCCGGGAT CTCAGGGATT GCGAGCCAAC GCGCGGCCCG AAAAATAAC AATTGAGTAC AAATGTCGA ATAGTAGCTA
477 P G K O
^start lambda t0 terminator ^end lambda t0 terminator
^start of tet resistance promoter ^-35 of promoter
3101 AAGCTTTAAT GCGGTAGTTT ATCACAGTTA AATTGCTAAC GAGTCAGGC ACCGTGTATG AAATCTAACA ATGCGTCTAT CGTCATCCTC GGCACCCGTC
TTCGAAATTA CGCCATCAA TAGTGCAAT TTAACGATG CGTCAGTCCG TGGCACATAC TTTAGATTGT TACGCGAGTA GCAGTAGGAG CCGTGGCAGT
^-10 region of tet resistance promoter ^start of tet resistance translation
3201 CCCTGGATGC TGTAGGATA GGCTTGGTTA TGCCGGTACT GCCGGCCTC TTGCGGGATA TCGTCCATTC CGACAGCATC GCCAGTCACT ATGCGGTGCT
GGGACCTACG ACATCCGTAT CCGAACCAAT ACGGCCATGA CGGCCCGGAG AACGCCCTAT AGCAGGTAAG GCTGTCTAG CGTCTAGTGA TACCGCACGA
3301
```

FIG. 19A

1 GAATTCAACT TCTCCATCT TTGGATAAGG AATATACAGAC ATGAAAAATC TCATTGCTGA GTTGTATT TT AAGTTGCC AAAAAGAAGA AGAGTCGAAT
CTTAAGTTGA AGAGGTATGA AACCTATTCC TTTATGTCGT TACTTTTAG AGTAACGACT CAACAATAAA TTCGAACGGG TTTTCTTCT TCTCAGCTTA

101 GAACGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACACGG GTTGATTGAT CAGGTAGAGG
CTTGACACAC GGTCCATCT TCGAAACCTC TAATAGCAGT GACGTACGA AGGTTATAC CCGTTTTTAC TGGTTGTGCG CAACTAACTA GTCCAICTCC

201 GGGCGCTGTA CGAGGTAAG CCGATGCCA GCATTCCTGA CGACGATAG GAGTCTGTC GCGATTACGT AAAGAAGTTA TTGAAGCATC CTCGTCACTA
CCCGGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA TTTCTTCAAT AACTTCGTAG GAGCAGTCAT

301 AAAAGTTAAT CTTTCAACA GCTGTCATAA AGTTGTACAG GCCGAGACTT ATAGTCGCTT TGTTTTTTATT TTTTAATGTA TTGTAACTA GTACGCAAGT
TTTTCAATTA GAAAGTTGT CGACAGTATT TCAACAGTGC CGGCTCTGAA TATCAGGAA ACAAAATAA AAAATTACAT AAACATTGAT CATGCGTTCA

401 TCACGTAAAA AGGGTATCTA GAATTATGAA GAAGAATATC GCATTTCTTC TTGCATCTAT GTTCGTTTTT TCTATTGCTA CAAACGCTA CGCTGATATC
AGTGCATTTT TCCCATAGAT CTTAATACTT CTTCTTATAG CGTAAGAAG AACGTAGATA CAAGCAAAA AGATAACGAT GTTTGGCAT GCGACTATAG

1 M K K I A F L L A S M F V F S I A T N A Y A D I
'STII Signal TIR -1 Anti-VEGF Light chain (version Y0317)^

501 CAGTTGACC AGTCCCGAG CTCCTGTCC GCCTCTGTGG CGATPAGGT CACCATCACC TGCAGCGCAA GTCAGGATAT TAGCAACTAT TTAACTGGT
GTCAACTGG TCAGGGCTC GAGGGACAG CGGACACACC CGCTATCCA GTGGTAGTG ACCTCGGCTT CAGTCCCTATA ATCGTTGATA AATTGACCA

26 Q L T Q S P S S L S A S V G D R V T I T C S A S Q D I S N Y L N W Y

601 ATCAACAGAA ACCAGGAAA GCTCCGAAAG TACTGATTTA CTTACCTCC TCTCTCCACT CTGGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC
TAGTTGTCTT TGGTCCCTTT CGAGGCTTTC ATGACTAAAT GAAGTGGAG AGAGAGGTGA GACCTCAGG AAGAGCGAAG AGACCTAGGC CAAGACCCCTG

60 Q Q K P G K A P K V L I Y F T S S L H S G V P S R F S G S G S G T

701 GGAITTCAT CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTGCA ACAGTATAGC ACCGTGCCGT GGACGTTTG ACAGGGTACC
CCTAAAGTGA GACTGTAGT CGTCAGAGT CGGTCTTCTG AAGCGTTGAA TAATGACGT TGTCAATCG TGGCACGCA CCTGCAACC TGTCCTCATG

93 D F T L T I S S L Q P E D F A T Y Y C Q Q Y S T V P W T F G Q G T

801 AAGTGGAGA TCAACGAAC TGTGGCTGCA CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT GTGTGCCCTG
TTCCACCTCT AGTTGCTTG ACACCGACGT GGTAGACAGA AGTAGAAGG CGGTAGACTA CTGCTCACT TTAGACCTTG ACGAAGACAA CACACGGACG

126 K V E I K R T V A A P S V F I P P S D E Q L K S G T A S V V C L L

901 TGAATPACTT CTATCCAGA GAGGCCAAAG TACAGTGGAA GGTGATAAC GGCCTCCAAT CCGGTAACTC CCAGGAGAT GTACAGAGC AGCAGACAA
ACTTATTGAA GATAGGTCT CTCGGTTTC ATGTCACCTT CCACCTATTG CCGGAGGTTA GCCCATTTAG GGTCTCTCA CAGTGTCTCG TCCTGTGCTT

160 N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K

FIG. 19B

1001 GGACAGACC TACAGCCTCA GCAGCACCTT GACGTGAGC AAAGCAGACT ACAGAGAAACA CAAAGTCTAC GCCTCGAAG TCACCCATCA GGGCCTGAGC
CCTGTCTGG ATGTCTGGAGT CGTCTGGGGA CTGCGACTCG TTTCGTCTGA TGCTCTTTGT GTTTCAGATG CGGACGCTTC AGTGGGTAGT CCGGACTCG
193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S
1101 TCGCCGTCA CAAAGAGCTT CAACAGGGGA GAGTGTAAAT TAAATCCTCT ACGCCGAGC CATCGTGGG AGCTCGGTAC CCGGGGATCT AGGCCTAACG
AGCGGGCAGT GTTCTCGAA GTTGTCCCT CTCACAATTA ATTTAGAGA TGGGGCTGC GTAGCACCGC TCGAGCCATG GGGCCCTAGA TCGGATTGC
226 S P V T K S F N R G E C O
1201 CTCGGTGGC GCGGGCGTT TTTTATTGTT GCCGACGGC ATCTGAATG AACTGTGTGC GCAGGTAGAA GCTTTGGAGA TTATCGTCAC TGCAATGCTT
GAGCAACGG CGGCCCGCAA AAAATAACAA CCGCTGCGG TAGAGTTAC TTGACACAGC CGTCCATCTT CGAAACCTCT AATAGCAGTG ACGTTACGAA
1301 CGCAATATG CGCAAAATGA CCAACAGCG TTGATTGATC AGGTAGAGG GCGCTGTAC GAGTAAAGC CCGATGCCAG CATTCCTGAC GAGCATACGG
CGGTATACC GCGTTTACT GGTGTGCGC AACTAACTAG TCCATCTCC CCGCAGCATG CTCCATTTCC GGCTAGGTC GTAAGGACTG CTGCTATGCC
1401 AGCTGCTGG CGATTACGTA AAGAAGTTAT TGAAGCATCC TCGTCAGTAA AAGTTAATC TTTTCAACAG CTGTCAATAA GTTGTACCG CCGAGACTTA
TCGACGACG GCTAATGCAT TTCTTCAATA ACTTCGTAGG AGCAGTCAIT TTTCATATAG AAAGTTGTC GACAGTATTT CAACAGTGCC GGCTCTGAAT
1501 TAGTCGCTTT GTTTTATTT TTTAATGTAT TTGTAACATG TACGCAAGT CAGTAAAAA GGGTATCTAG AATTATGAG AAGAATATCG CATTCCTCT
ATCAGGAAA CAAAATAAA AAATTACATA AACATTGATC ATGCGTTCAA GTGCAITTTT CCCATATGTC TTAATCTTC TTCTTATAGC GTAAAGAAGA
1 M K K N I A F L L
*Still Signal TIR-1
1601 TGCACTATG TTCTGTTTTT CTATTGCTAC AAACGCTGAC GCTCAGTTC AGCTGGTSCA GTCTGGCGCA GAGTGAATAA AGCCAGGGC TTCAGTTAAA
ACGTAGATAC AAGCAAAAA GATAACGATG TTTGGGATG CGAGTCCAAG TCAGCACAGT CAGACCGGT CTCCACTTTT TCGGTCCCG AAGTCAATTT
10 A S M F V F S I A T N A Y A Q V Q L V Q S G A E V K K P G A S V K
*Anti-VEGF (version Y0317) Heavy Chain
*Heavy Chain FR1 changed to SubgroupI consensus sequence
1701 GTATCTGTA AAGCTTCTGG CTACGACTTC ACGCACTAGC GTATGAACTG GGTCCGTAC GCGCCGGTA AGGCGTGA ATGGGTGGA TGGATTACA
CATAGACAT TTCGAAGACC GATCTGAAG TCGGTGATGC CATCTGAC CCAGGCAGTC CCGGGCCCAT TCCCGACCT TACCCAACT ACCTAATGT
43 V S C K A S G Y D F T H Y G M N W V R Q A P G K G L E W V G W I N T
1801 CCTATACCG TGAACCGACC TATGCTGCG ATTTCAAAG TCGTTTCACT TTTTCTTTAG ACACCTCAA AAGCACAGCA TACCTGCAGA TGAACAGCCT
GGATATGCC ACTTGGCTG ATACGAGCC TAAAGTTTGC AGCAAGTGA AAAGAATC TGTCGAGGT TTCTGTCTCT ATGGAGCTCT ACTTGTGGA
77 Y T G E P T Y A A D F K R R F T F S L D T S K S T A Y L Q M N S L
1901 GCGCGCTGAG GACACTGCCG TCTATTACTG TGCAAAATAC CCGTACTATT ATGGGACGAG CCACTGGTAT TTCTGAGCTCT GGGGTCAAG AACCTGGTC
CGCGGACTC CTGTGACGC AGATAATGAC ACGTTTATG GGCATATAA TACCTCTCTC GGTGACCAT AAGCTGCAGA CCCCAGTTCC TTGGGACCCAG
110 R A E D T A V Y Y C A K Y P Y Y Y G T S H W Y F D V W G Q G T L V
2001 ACCGTCTCCT CGGCTTCCAC CAAGGGCCCA TCGGTCTTCC CCGTGCACC CTCTCTCAAG AGCACCTCTG GGGCCACAGC GGGCTGGG TGCCTGGTCA
TGGCAGAGA GCGGAGGTG GTTCCCGGT AGCCAGAGG GGGACCGTGG GAGGAGTTC TCGTGGAGC CCCCCTGTG CCGGGACCCG ACGGACCACT
143 T V S S A S T K G P S V F P L A P S S K S T S G G T A A L G C L V K

FIG. 19C

2101 AGGACTACTT CCCGAACCG GTGACGGTGT CGTGAACCT AGGCCCTTG ACCAGGGCG TGCACACCTT CCCGCTGTC CTACAGTCTT CAGGACTCTA
TCCTGATGAA GGGGCTTGGC CACTGCCACA GCACCTTAG TCCGGGGGAC TGGTCGCCG ACGTGTGAA GGGCGGACAG GATGTCAGGA GTCTGTGAT
177 D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S G L Y
2201 CTCCCTCAGC AGCGTGGTGA CTGTGCCCTC TAGCAGCTTG GGCACCCAGA CCTACATCTG CAAGTGAAT CACAAGCCCA GCAACACCAA GGTGGACAAG
GAGGAGTGG TCGCACCACT GACACGGGAG ATCGTGAAC CCGTGGTCT GGATGTAGAC GTTGCACCTA GTGTTCGGT COTGTGGTT CCACCTGTTC
210 S L S S V V T V P S S S L G T Q T Y I C N V N H K P S N T K V D K
2301 AAAGTTGAGC CCAATCTTG TGACAAACT CACATATGCC CACCGTGCC AGCACCCTGAA CTCTGGGGG GACGTCAGT CTCTCTTTC CCCCCAAAAC
TTTCAACTCG GGTTTAGAAC ACTGTTTGA GTGTGTACGG GTGGACGGG TCGTGACTT GAGGACCCCT CTGGCAGTCA GAAGGAGAAG GGGGTTTTG
243 K V E P K S C D K T H T C P P C P A P E L L G G P S V F L F P P K P
2401 CCAAGGACAC CCTCATGATC TCCCGGACCC CTGAGGTAC ATCGTGGTG GTGGACGTGA GCCACGAAGA CCCTCAGGTC AAGTCAACT GGTACGTGGA
GGTTCCTGTG GGAGTACTAG AGGGCCTGGG GACTCCAGTG TACGCACCAC CACTGCACT CGTGCTTCT GGGACTCCAG TTCAAGTTGA CCATGCACCT
277 K D T L M I S R T P E V T C V V V D V S H E D P E V K F N W Y V D
2501 CGGCGTGGAG GTGCATAATG CCAAGACAAA GCCGGGGAG GAGCAGTACA ACAGCAGCTA CCCTGTGTC AGCTCTCTCA CGTCTCTGCA CCAGGACTGG
GCCGACCTC CACGTATTAC GGTCTCTTT CGGCGCCCTC CTCGTCATGT TGTCTGTCAT GGCACACCAG TCGCAGGAGT GGCAGGACGT GGTCTCTGACC
310 G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H Q D W
2601 CTGAATGGCA AGGAGTACAA GTGCAAGGTC TCCAACAAG CCCTCCAGC CCCCCTCGAG AAAACCATCT CCAAGCCAA AGGGCAGCCC CGAGAACCAC
GACTTACCTT TCCTCATGTT CAGGTTCCAG AGGTTGTTT CCGAGGGTGG GGGTAGCTC TTTTGTAGA GGTTCGGT TCCCGTCGG GCTCTTGGT
343 L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R E P Q
2701 AGGTGTACAC CCTGCCCCCA TCCCGGGAAG AGATGACCAA GAACCAAGTC AGCTGACCT GCCTGTCAA AGGTTCTAT CCCAGCGACA TCGCCGTGGA
TCCCATGTG GGACGGGGT AGGCCCTTC TCTACTGTT CTGTGTCAG TCGGACTGGA CGGACCACTT TCCGAAGATA GGTCTCTGT AGCGGCACCT
377 V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I A V E
2801 GTGGAGAGC AATGGGAGC CGGAGAACAA CTACAAGACC AGCCCTCCG TCGTGGACTC CGACGGCTCC TTCTTCTCT ACAGCAAGCT CACGCTGGAC
CACCTCTCG TTACCGGTG GCCTCTTGT GATGTTCTG TCGGAGGGC ACACCTGAG GCTCCGAGG AAGAAGGAGA TGTCTGTCGA GTGCAACCTG
410 W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L T V D
2901 AAGACAGGT GGCAGCAGG GAAGTCTTC TCATGCTCG TGATCATGA GGCTCTGAC AACCACTACA CGCAGAAGAG CCTCTCCCTG TCTCCGGTA
TTCTCGTCCA CGTCTCTCC CTTGCAGAAG AGTACGAGC ACTAGTACT CCAGACGTG TTGTGTATGT GCGTCTTCTC GGAGAGGAC AGAGGCCCAT
443 K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S P G K
3001 AATAAGCATG CGACGGCCCT AGAGTCCCTA ACCTCTGTT GCCCGGGG GTTTTTATT GTTAATCAT GTTTCACAGC TTATCATCGA TAAGCTTAA
TTATTCTGAC GCTGCCGGA TCTCAGGAT TCGAGCCAA CGCGGCCCG CAAAAATAA CAATTGAGTA CAACTGTG AATAGTAGCT ATTCGAAAT
477 O
3101 TCGCGTAGTT TATCAGATT AAATTGCTAA CGCAGTCAGG CACCGTAT GAAATCTAAC AATCGCTCA TCGTCATCTT CGGCACCGTC ACCCTGGATG
ACGCCATCAA ATAGTGTCAA TTTAACGATT CGGTCACTCC GTGGACATA CTTTAGATT TTACCGAGT AGCAGTAGGA GCCGTGGCAG TGGACCTTAC
^Start Tet Resistance Coding Sequence

FIG. 19D

3201 CTGTAGGCAT AGGCTTGGTT ATGCCGGTAC TGCCGGGCTT CTTGCGGGAT ATCGTCCATT CCGACAGCAT CGCCAGTCAC TATGGCGTGC TGCTAGCGCT
GACATCCGTA TCCGAACCAA TAGGGCCATG ACGGCCCCGA GAACGCCCTA TAGCAGGTAA GGCTGTGTA GCGGTCAGTG ATACCCACG ACGATCGGGA

3301

FIG. 20A

1 GAATTCAACT TCTCCATACT TTGGATAAGG AATACACAGAC ATGAAAAATC TCATTGCTGA GTTGTATT TT AAGTTGTGCC AAAAAAGA AGAGTCGAAT
CTTAAGTTGA AGAGGTATGA AACCTATTCC TTTATGCTGT TACTTTTTAG AGTAACGACT CAACAATAAA TTCGAACGGG TTTTCTTCT TCTCAGCTTA

101 GAACTGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATGCT TGGCAATATG GCGCAAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAGG
CTTGACACAC GCGTCCATCT TCGAAACCTC TAATAGCAGT GACGTTACGA AGGTTATATC CCGTTTTTAC TGGTTGTGCG CAACTAACTA GTCCATCTCC

201 GGGCGCTGTA CGAGGTPAAAG CCGATGCCA GCATTCTCTGA CGACGATACG GAGCTGTGTC GCGANTAGCT AAAGAAGTTA TTGAAGCATC CTCGTAGTA
CCCGGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GCTGTATGTC CTCGACGACG CGCTAATGCA TTTCTTCAAT AACTTCGTAG GACGAGTCAT

301 AAAAGTTAAT CTTTCAACA GCTGTCTATA AGTTGTACAG GCCGAGACTT ATAGTCGCTT TGTTTTTATT TTTTAATGTA TTGTAACTA GTACGCAAGT
TTTTCAATTA GAAAGTTGT CGACAGTATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA ACAAATAA AAAATTACAT AAACATTGAT CATGCGTTCA

401 TCACGTAAAA AGGTATCTTA GAATTATGAA GAAGAATATC GCATTCTTTC TTGCACTAT GTTCGTTTTT TCTATTGCTA CAAACGCGTA CGCTGATATC
AGTGCATTTT TCCCATAGAT CTTAATACTT CTTCCTTATAG CGTAAAGAAG AAGCTAGATA CAAGCAAAA AGATAACGAT GTTTGCGCAT GCGACTATAG

1 M K K N I A F L L A S M F V F S I A T N A Y A D I
anti-IgE light chain^{*}
^{*}STII signal TIR-1

501 CAGGTGACCC AGTCCCGGAG CTCCTGTGCC GCCTGTGG GCGATAGGT CACCATCACC TGGCGTGCCA GTCAGAGCGT CGATTAGGAT GGTGATAGCT
GTGCACTGGG TCAGGGGCTC GAGGACAGG CGGAGACACC CGCTATCCCA GTGGTAGTGG ACGSCACGGT CAGTCTCGCA GCTAATGCTA CCACTATCGA

26 Q L T Q S P S S L S A S V G D R V T I T C R A S Q S V D Y D G D S Y

601 ACATGAAC TGATCAACAG AAACAGGAA AAGCTCCGAA ACTACTGATT TAGCGGSCCT CGTACCTGGA GTCTGGAGTC CCTTCTCGCT TCCTCTGGATC
TGTACTTGAC CATAGTTGTC TTTGGTCCCTT TTCGAGGCTT TGATGACTAA ATGCGCCGGA GCATGGACCT CAGACCTCAG GGAAGAGCGA AGAGACCTAG

60 M N W Y Q Q K P G K A P K L L I Y A A S Y L E S G V P S R F S G S

701 CGGTTCTGGG ACGGATTTCA CTCTGACCAT CAGCAGTCTG CAGCCGGAAG ACTTCGCAAC TTATTACTGT CAGCAAAATC ACGAGGATCC GTACACATTT
GCCAGACCC TGCCTAAAGT GAGACTGGTA GTCGTCAGAC GTCGGCTTC TGAAGCGTTG AATAATGACA GTCGTTTCAG TGCTCCTAGG CATGTGTAAG

93 G S G T D F T L T I S S L Q P E D F A T Y Y C Q Q S H E D P Y T F

801 GGACAGGTA CCAAGGTGA GATCAACGA ACTGTGGCTG CACCATCTGT CTTTCATCTC CCGCCATCTG ATGACAGTT GAAATCTGGA ACTGCCTCTG
CCTGTCCCAT GGTCCACCT CTAGTTTGCT TGACACCCAC GTGGTAGACA GAAGTAGAAG GCGGTAGAC TACTCGTCAA CTTTAGACCT TGACGGAGAC

126 G Q G T K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V

901 TTGTGTGCTT GGTGAATAAC TTCTATCCCA GAGAGGCCAA AGTACAGTGG AAGGTCCTCA ACGCCTCCA ATCGGGTAAC TCCAGGAGA GTGTACAGA
AACACACGA CGACTTATTG AAGATAGGCT CTCCTCCGTT TCATGTCACC TTCCACCTAT TGCGGGAGGT TAGCCCATTG AGGGTCTCT CACAGTGTCT

160 V C L L N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E

FIG. 20B

1101 GCAGGACAGC AAGGACAGCA CCTACAGCCT CAGCAGCACC CTGAGCCTGA GCAAAGCAGA CTACGAGAAA CACAAGTCT ACGCCTGCGA AGTACCCAT
CGTCTGTGCG TTCCTGTGCT GGATGTCGGA GTGCTGCTGG GACTGGGACT CGTTTCGTCT GATGCTCTTT GTGTTTCAGA TCGGGAGCGT TCAGTGGGTA
193 Q D S K D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H
1101 CAGGSCCTGA GCTCGCCCGT CACAAAGAGC TTCAACAGGG GAGAGTGTTA ATTAAATCCT CTACGCCGGA CGCATCGTGS CGAGCTCGGT ACCCGGGGAT
GTCCCGGACT CGAGCGGGCA GTGTTTCTCG AAGTTGTGCC CTCTACAAT TAATTTAGGA GATCGGCGCT GCGTAGCACC GCTCGAGCCA TGGGCCCCCTA
226 Q G L S S P V T K S F N R G E C O
1201 CTAGGCCTAA CGCTCGGTTG CGGCCGGGCG TTTTATTG TGCCGAGCG GCATCTGAA TGAATGTGT GCGCAGGTAG AAGCTTTGGA GATTATCGTC
GATCCGGATT GCGAGCCAAC GCGGCCCGCG AAAAATAAC AACGGTGGC CGTAGAGCTT ACTTGACACA CGGTCCATC TTCGAAACCT CTAATAGCAG
1301 ACTGCAATGC TTGCAATAT GCGCAAAAT GACCAACAGC GGTGATTGA TCAGGTAGAG GGGCGGCTGT ACGAGGTAAA GCCCGATGCC AGCATTCCTG
TGACGTTACG AAGCGTTATA CCGGTTTTA CTGGTTGTCG CCACTAACT AGTCCATCTC CCGCGGACA TGCTCCATTT CGGGCTACGG TCGTAAGGAC
1401 ACGACGATAC GGAGCTGCTG CCGGATTACG TAAAGAAGTT ATTGAAGCAT CCTGCTCAGT AAAAAGTTAA TCTTTTCAAC AGTGTGCATA AAGTTGTCAC
TGCTGCTATG CCTCGACGAC GCGCTAATGC ATTTCTTCAA TAACITCGTA GGAGCAGTCA TTTTTCATTT AGAAAAGTTG TCGACAGTAT TTCAACAGTG
1501 GGCCGAGACT TATAGTCGCT TTGTTTTTAT TTTTAAATGT ATTTGTAAT AGTAGGCAAG TTCACGTAAA AAGGTATCT AGAATTATGA AGAAGAATAT
CCGGCTCTGA ATATCAGCGA AACAAAAATA AAAAATTACA TAAACATTGA TCATGCTTIC AAGTGCAATT TTCCCATAGA TCTTAATACT TCTTCTTATA
M K K N I
1 ^STII Signal TIR-1
1601 CGCATTTCTT CTGCACTA TGTTCGTTTT TTCTATTGCT ACAACGCGT ACCTGAGGT TCAGTGTGT GAGTCTGGG GTGGCCTGGT GCAGCCAGGG
GCGTAAGAA GAACGTAGAT ACAAGCAAA AAGATAACGA TGTTCGCGA TGGGACTCCA AGTCAGCAC CTCAGACCGC CACCGGACCA CGTCGGTCCC
6 A F L L A S M F V F S I A T N A Y A E V Q L V E S G G L V Q P G
^anti-IgE heavy chain
1701 GGCTCACTCC GTTGTCTCTG TGCAGTTTCT GGCTACTCCA TCACCTCCGG ATATAGCTGG AACTGGATCC GTCAGCCCG GGTAAAGGC CTGGAATGGG
CCGAGTGAGG CAACAGGAC ACGTCAAGA CCGATGAGT AGTGAGGCC TATATCGACC TTGACCTAGG CAGTCCGGG CCCATTCCCG GACCTTACCC
39 G S L R L S C A V S G Y S I T S G Y S W N W I R Q A P G K G L E W V
1801 TTGCATCGAT TACGTATGAC GGATCGACTA ACTATAACCC TAGCGTCAAG GGCGGTATCA CTATAAGTCG CGACGACTCC AAAAACACAT TCTACCTGCA
AACGTAGCTA ATGCATACTG CCTAGCTGAT TGATATTGG ATCGAGTTT CCGGCATAGT GATATTCAGC GCTGTGAGG TTTTGTGTA AGATGGACGT
73 A S I T Y D G S T N Y N P S V K G R I T I S R D D S K N T F Y L Q
1901 GATGAACAGC CTGCGTCTG AGGACACTGC CGTCTATTAT TGTGTCGAG GCAGCCACTA TTTCCGTGTC TGGCACTTCG CCGTGTGGG TCAAGGAACC
CTACTGTGCG GAGGACGAC TCCTGTGACG GCAGATAATA ACACGAGCTC CGTCGGTGAT AAAGCCAGT ACCGTGAAGC GGCACACCCC AGTTCCTTGG
106 M N S L R A E D T A V Y Y C A R G S H Y F G H W H F A V W G Q G T
2001 CTGGTCAACG TCTCCTCGG CTCACCAAG GGCCCATCGG TCTTCCCCCT GGCAACCTCC TCCAAGACA CCTCTGGGG CACAGCGGCC CTGGGCTGCC
GACCAGTGGC AGAGGAGCGG GAGGTGTTTC CCGGTAGCC AGAAGGGGA CCGTGGGAGG AGGTTCCTGT GGAGACCCCC GTGTGCGCGG GACCCGACGG
139 L V T V S S A S T K G P S V F P L A P S S K S T S G G T A A L G C L

FIG. 20C

2101 TGTCTAAGGA CTACTTCCCC GAACGGGTGA CGGTGCTGT GAACTAGGC GCCTGACCA CGGGCGTGA CACCTTCCCG GCTGTCTTAC AGTCCTCAGG
ACCAGTTCCT GATGAAGGG CTTGGCCACT GCCACAGCAC CTTGAGTCCG CGGACTGGT CGCCGACCGT GTGGAAGGC CGACAGATG TCAGGAGTCC
173 V K D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S G
2201 ACTTCTACTCC CTCAGCAGCG TGGTGACTGT GGCCTTAGC AGCTTGGCA CCACAGACCTA CATCTGCAAC GTGAATCACA AGCCAGCAA CACCAGGTG
TGAGATGAGG GAGTCGTGCG ACCACTGACA CGGGAGATCG TCGAACCCGT GGGTCTGATG GTAGAGTTG CACTAGTTGT TCGGGTCTGT GTGGTTCCAC
206 L Y S L S S V V T V P S S S L G T Q T Y I C N V N H K P S N T K V
2301 GACAAGAAAG TTGAGCCCAA ATCTTGTGAC AAACTCACA CATGCCACC GTGCCACCA CTTGAACCTC TGGGGGACC GTCACTCTTC CTCTTCCCCC
CTGTTCTTTC AACTCGGGTT TAGACACTG TTTTGAGTGT GTACGGTGG CACGGTGGT GAGCTGAGG ACCCCCTGG CAGTCAGAAG GAGAAGGGG
239 D K K V E P K S C D K T H T C P P C P A P E L L G G P S V F L F P P
2401 CARAAACCAA GGACACCCTC ATGATCTCCC GGACCCCTGA GGTACATGC GTGTGTGGT ACGTGAGCCA CGAAGACCCT GAGTCAAGT TCAACTGGTA
GTTTGGTTT CCTGTGGAG TACTAGAGG CTTGGGACT CCACTGTACG CACCACCACC TGCATCTGGT GCTTCTGGGA CTCCAGTTCA AGTTGACCAT
273 K P K D T L M I S R T P E V T C V V V D V S H E D P E V K F N W Y
2501 CGTGGACGGC GTGAGGTGC ATAATGCCAA GACAAAGCCG CGGAGGAGC AGTACAACG CAGCTACCGT GTGGTCAGC TCCTCACCGT CCTGCACCAG
GCACCTGCC CACCTCCAG TATTACGGTT CTGTTTCGGC GCCCTCTCCG TCATGTTGC GTGCATGGCA CACCACTGC AGGAGTGGCA GGACGTGGTC
306 V D G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H Q
2601 GACTGGCTGA ATGCAAGGA GTACAAGTGC AAGGTCTCCA ACAAGCCCT CCCAGCCCC ATCGAAGAAA CCACTCCAA AGCCAAAGG CAGCCCCGAG
CTGACCGACT TACGTTCTCT CATGTTACG TTCCAGAGT TGTTTCGGGA GGGTCGGGG TAGCTCTTTT GGTAGAGTT TCGGTTTCCC GTCCGGGCTC
339 D W L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R E
2701 AACACACAGT GTACACCCTG CCCCATCCC GGAAGAGAT GACCAAGAC CAGTCAAGC TGACCTGCCT GGTCAAAGG TTCTATCCA GGCACATCGC
TTGGTGTCCA CATGTGGAC GGGGTAGG CCGTTCTCTA CTGTTCTCTA GTCCAGTCG ACTGGACGGA CCAGTTTCCG AAGATAGGT CGCTGTAGCG
373 P Q V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I A
2801 CGTGGAGTGG GAGACCAATG GGCAGCCGA GAACAACATC AAGACCAGC CTCCGCTGT GAGCTCCGAC GGCTCCTTCT TCCTCTACAG CAAGTCAACC
GCACCTCACC CTCTCGTTAC CCGTCGGCCT CTGTGTTGATG TTCTGGTGG GAGGCACCA CTTGAGCTG CCAGGGAAGA AGGAGATGTC GTTCGAGTGG
406 V E W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L T
2901 GTGACACAAGA GCAGGTGGA GCAGGGAAC GTCTTCTCAT GCTCCGTGAT GCATGAGGT CTGCAACAAC ACTACACGCA GAAGAGCCTC TCCTGTCTC
CACCTGTCT CGTCCACCGT CGTCCCTTG CAGAAGATA CGAGCATA CGTACTCCA GAGCTGTGG TGATGTGGT CTCTCCGAG AGGGACAGAG
439 V D K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S P
3001 CGGTAATAA AGCATGGAC GGCCTAGAG TCCTTAACG TCGTTGGC CGGGGGTTT TTTATTGTTA ACTCATGTTT GACAGCTTAT CATCGATAAG
GCCCATTTAT TCGTACGCTG CCGGATCTC AGGATTTGCG AGCCAACGG GGGCCGCAA AATAACAAT TGAGTACAAA CTGTCCAATA GTAGCTATT
473 G K O
3101 CTTTAAATCG GTAGTTTATC ACAGTTAAAT TGCTAAGCA GTCAAGGACC GTGTATGAA TCTAACAAT CGTCACTCGT CATCTCCGG ACCGTCAACC
GAAATTACGC CATCAAAATG TGTCAATTTA ACGATTGGT CAGTCCGTTG CACATACTT AGATTGTTAC GCGAGTAGCA GTAGGAGCCG TGGCAGTGGG

FIG. 20D

3201 TGGATGCTGT AGGCATAGGC TTGGTTATGC CGGTACTGCC GGGCCTCTTG CGGGATATCG TCCATTCCGA CAGCATCGCC AGTCACTATG GCGTCTGCT
ACCTACGACA TCCGTATCCG AACCAATACG GCCATGACGG CCGGAGAAC GCCCTATAGC AGGTAAGGCT GTCGTAGCGG TCAGTGATAC CGCAGACGA

3301

FIG. 21A

1 GAATCAACT TCTCCATACT TTGGATAAGG AATACAGAC ATGAATAAT TCATTGCTGA GTTGTTATT AAGTTGCCC AAAAAGAAGA AGATCGAAT
CTTAAGTTGA AGAGGTATGA AACCTATTCC TTTATGCTG TACTTTTAG AGTAACGACT CAACAATAA TTCGAACGGG TTTTCTTCT TCTCAGCTTA

101 GAACTGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATGCT TCCCAATATG GCGCAAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAGG
CTTGACACAC GCGTCCATCT TCGAAACCTC TAATAGCAGT GACGTTACGA AGGTTATAC CGCGTTTAC TGGTTGTGCG CAACTRAATA GTCCATCTCC

201 GGGCGCTGTA CGAGGTAAAG CCGATGCCA GCATTCCTGA CGAGNATAG GAGCTGCTG GCGATTAGT AAAGAAGTTA TTGAAGCATC CTCGTCAGTA
CCCGCGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA TTTCCTCAAT AACCTCGTAG GAGCAGTCAT

301 AAAAGTTAAT CTTTCAACA GCTGTCATAA AGTTGTCAGG GCGGACACT ATAGTCGCTT TGTTTTATT TTTTAATGTA TTGTAACTA GTACGCAAGT
TTTTCAATTA GAAAGTTGT CGACAGTATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA ACAAAATAA AAAATTACAT AAACATTGAT CATCGGTCA

401 TCACGTAAA AGGTATCTA GAATTATGAA GAAGATATC GCATTTCTTC TTGCATCTAT GTTCGTTTT TCTATTGCTA CAAACGGTA CGCTGATATC
AGTGCAATTT TCCCATAGAT CTTAATACTT CTTCTTATAG CGTAAGAAG AACGTAGATA CAAGCAAAA AGATAACGAT GTTTGCGCAT GCGACTATAG

1 M K K N I A F L L A S M F V F S I A T N A Y A D I
^STII signal TIR-1 anti-IgE light chain^

501 CAGCTGACCC AGTCCCGAG CTCCTGTCC GCTCTGTGG GCGATAGGT CACCATCAC TGCCGTGCCA GTCAGAGCGT CGATTACGAT GGTATAGCT
GTCGACTGG TCAGGGGCTC GAGGGACAGG CGGAGACACC CGCTATCCCA GTGGTAGTG ACAGCACCGT CAGTCTCGCA GCTAATGCTA CCACTATCGA

26 Q L T Q S P S L S A S V G D R V T I T C R A S Q S V D Y D G D S Y

601 ACATGAACTG GTATCAACAG AAACCAAGAA AAGTCCGAA ACTACTGATT TAGCGGCGCT CGTACCTGGA GTCTGGAGTC CTTCTCGCT TCTCTGGATC
TGTAATTGAC CATAGTTGTC TTGGTCTCTT TTCGAGGCTT TGATGACTAA ATCGGCCGGA GCATGGACCT CAGACCTCAG GGAAGACGGA AGAGACCTAG

60 M N W Y Q K P G K A P K L L I Y A A S Y L E S G V P S R F S G S

701 CGGTTCTGG ACGATTTCA CTCGACCAT CAGAGTCTG CAGCCGGAAG ACTTCGCAAC TTATTACTGT CAGCAAGTC ACGAGGATCC GTACACATTT
GCCAGACCC TGCTAAAGT GAGACTGGTA GTCGTGAGC GTCGGGCTTC TGAAGCGTTG AATAATGACA GTCGTTTCAG TGCCTCTAGG CATGTGTAAA

93 G S G T D F T L T I S S L Q P E D F A T Y Y C Q Q S H E D P Y T F

801 GGACAGGTA CCAAGGTGA GATCAACGA ACTGTGGCTG CACCATCTGT CTTTATCTTC CCGCATCTG ATGAGCAGTT GAAATCTGGA ACTGCCTCTG
CCTGTCCCAT GGTTCACCT CTAGTTTGCT TGACACCGAC GTGGTAGACA GAAGTAGAAG GCGGTAGAC TACTCGTCAA CTTTAGACCT TGACGGAGAC

126 G Q G T K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V

901 TTGTGCTGCT GCTGAATAAC TTCTATCCCA GAGAGGCCAA AGTACAGTGG AAGGTGATA ACGCCCTCCA ATCGGGTAAC TCCAGGAGA GTGTACAGTA
AACACACGA CGACTTATTG AAGATAGGT CTCTCGGTT TCATGTCACC TTCCACCTAT TGCGGAGGT TAGCCATTG AGGGTCTCT CACAGTGTCT

160 V C L L N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E

FIG. 21B

1101 GCAGACAGC AAGACAGCA CCTACAGCCT CAGCAGCACC CTGACGCTGA GCAAGCAGA CTACGAGAAA CACAAGTCT AGCCTGCGA AGTCACCCAT
CGTCTGTGCG TTCCTGTGCT GATGTGCGGA GTGCTGCTGG GACTCGGACT CGTTTCGTCT GATGCTCTTT GTGTTTCAGA TCGGAGCGCT TCAGTGGGTA
193 Q D S K D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H

1101 CAGGSCCTGA GCTCGCCCGT CACAAAGAGC TTCAACAGG GAGAGTGTTA ATTAAATCCT CTAGCGCGA CGCATCGTGG CGAGCTCGGT ACCCGGGGAT
GTCCGGGACT CGAGCGGGA GTGTTTCTCG AAGTGTCTCC CTCTCACAAT TAATTTAGGA GATCGCGCCT GCGTAGCACC GCTCGAGCCA TGGGCCCCTA
226 Q G L S S P V T K S F N R G E C O

1201 CTAGGCCTAA CGCTCGGTTG CGCCCGGGCG TTTTATTATG TTGCCGACGC GCACTCGAA TGAACGTGTG GCGAGGTAG AAGCTTTGGA GATTATCGTC
GATCCGGATT GCGAGCCAAC GCGGCGCCGC AAAAATPAC AACGCTGGC CGTAGAGCTT ACTTGACACA GCGGTCCATC TTCGAAACCT CTAATAGCAG

1301 ACTGCAATGC TTCGCAATAT GCGCGAAAAT GACCAACAGC GGTGATTGA TCAGGTAGAG GGGCGCTGT ACAGGTAAA GCCCGATGCC AGCATTCCTG
TGCGTTAG AAGCGTTATA CCGCGTTTIA CTGGTTGTCG CCACTAAT AGTCCATCTC CCGCGGACA TGCTCCAATT CCGGCTACGG TCGTAAGGAC

1401 ACGAGGATAC GGAGTGTGCT GCGGATTACG TAAAGAATT ATTGAAGCAT CCTGCTCAGT AAAAAGTAA TCTTTTCAAC AGCTGTCATA AGTTGTGTCAC
TGCTGCTATG CCTCGACGAC GCGCTAATGC ATTCTTCAA TAACCTCGTA GGAGCAGTCA TTTTCAATT AGAAAAGTTG TCGACAGTAT TTCAACAGTG

1501 GGCCGAGACT TATAGTCGCT TTGTTTTTAT TTTTAAATGT ATTGTAAC AGTACGCAAG TTCACGTAAA AAGGTATCT AGAATTATGA AGAAGATAT
CCGCTCTGA ATATCAGCA AACAATAAATA AAAAATTACA TAAACATTGA TCATGCGTTC AAGTGCATTT TTCCATAGA TCTTAATCT TCTTCTTATA
M K K N I
1 ^STII Signal TIR-1

1601 CGCATTTCTT CTGCACTA TGTTCTGTTT TTCTATTGCT ACAAGCGCT AGCTCAGGT TCAGTCGAA GAGTCTGGC CGGCGCTGGT GAAACCATCT
GCGTAAAGAA GAACGTAGAT ACAAGCAAAA AAGATAACGA TGTTTGGCA TGGAGTCCA AGTGCAGCTT CTCAGACCG GCCCGGACCA CTTTGGTAGA
6 A F L L A S M F V F S I A T N A Y A Q V Q L Q E S G P G L V K P S
^anti-IgE Heavy Chain
^Heavy Chain FRI=SubgroupII consensus sequence

1701 CAGACTCTT CCTGACTTG TACTGTTTCT GGCTACTCCA TCACCTCCG ATATAGCTGG AACTGGATCC GTCAGGCCCC GGGTAAGGGC CTGGAATGGG
GTCTGAGAGA GGAACCTGAAC ATGACAAAGA CCGATGAGGT AGTGGAGGCC TATATCGACC TTGACCTAGG CAGTCCGGG CCATTTCCCG GACCTTACCC
39 Q T L S L T C T V S G Y S I T S G Y S W N W I R Q A P G K G L E W V

1801 TTGCATCGAT TACGTATGAC GGATCGACTA ACTATAACCC TAGCGTCAAG GCGCGTATCA CTATAAGTCG CGACGACTCC AAAACACAT TCTACCTGCA
AAGTAGCTA ATGCATACTG CCTAGCTGAT TGATATTGGG ATCGAGTTT CCGGCATAGT GATATTACG GCTGCTGAGG TTTTCTGTA AGATGGAGCT
73 A S I T Y D G S T N Y N P S V K G R I T I S R D D S K N T F Y L Q

1901 GATGACAGC CTGCGTGTGCT AGGACACTGC CGTCTATTAT TGTGCTGAG GCAGCCACTA TTTTCGTTCAC TGGCACTTCG CGGTGTGGG TCAAGGAACC
CTACTGTGCG GACGACAGC TCCTGTGACG GCAGATAATA ACACAGCTC CGTCGGTAT AAAGCCAGTG ACCGTGAAG GCACACCCC AGTTCTCTGG
106 M N S L R A E D T A V Y Y C A R G S H Y F G H W H F A V W G Q G T

2001 CTGCTACCG TCTCTCTGCG CTCACCAAG GGCCCATCGG TCTTCCCTT GGCACTCTCC TCCAAGACA CCTTGGGGG CACAGCGGC CTGGGCTGCC
GACAGTGGC AGAGGACCG GAGTGTGTTT CCGGTAGCC AGAAGGGGA CCGTGGAGG AGTTCTCTGT GGAGACCCC GTGTCGCCG GACCCGACGG
139 L V T V S S A S T K G P S V F P L A P S S K S T S G G T A A L G C L

FIG. 21C

2101 TGGTCAAGGA CTACTTCCCC GAACGGGTGA CGGTGCTGTG GAACTCAGGC GCCCTGACCA CGCGGTGCA CACCTTCCCG GTGTCTCTAC AGTCTCAGG
ACCAGTTCCT GATGAAGGG CTTGGCCACT GCCACAGCAC CTGTAGTCCG CGGACTGGT CGCCGACCT GTGGAAGGC CGACAGGATG TCAGAGTCC
173 V K D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S G
2201 ACTCTACTCC CTCAGCAGCG TGTGACTGT GCCCTTAGC AGCTTGGCA CCAAGACCTA CATCTGCAAC GTGAATCACA AGCCAGCAA CACCAAGTGT
TCAGATCAGG GAGTCGTGCG ACCACTGACA CGGGAGATCG TCGAACCCGT GGTCTGTGAT GTAGACGTG CACTTAGTGT TCGGGTCTGT GTGGTTCAC
206 L Y S L S S V V T V P S S S L G T Q T Y I C N V N H K P S N T K V
2301 GACAAGAAAG TTGAGCCCAA ATCTGTGAC AAACTCACA CATGCCACC GTGCCACCA CTTGAACTCC TGGGGGACC GTCACTCTTC CTCTTCCCC
CTGTTCTTTC AACTCGGGT TAGACACTG TTTTGTGTGT GTACGGTGT GTACGGTGT CACGGTGTG CACGGTGTG ACCCCCTGG CAGTCAGAAG GAGAAAGGGG
239 D K K V E P K S C D K T H T C P P C P A P E L L G G P S V F L F P P
2401 CAAACCCAA GGACACCCTC ATGATCTCCC GGACCCCTGA GGTACATGC GTGTGTGTG ACGTGAGCCA CGAAGACCCT GAGTCAAGT TCAACTGGTA
GTTTGGTTC CTTGTGGAG TACTAGAGG CTTGGGACT CCACTGTACG CACACACC CACACTCGT GCTTCTGGA CTCAGTTC AAGTGACCAT
273 K P K D T L M I S R T P E V T C V V V D V S H E D P E V K F N W Y
2501 CGTGGACGGC GTGAGGTGC ATAATGCCAA GACAAAGCCG CGGAGGAGC AGTACAACAG CACGTACCGT TGGTACGCG TCCTCACCGT CCTGCACCAAG
GCACCTGCG CACCTCCAG TATTACGGT TGTGTTGGC GCCTCTCTCG TCATGTTGTC GTGCATGGCA CACCACTGCG AGGAGTGGCA GGACGTGGTC
306 V D G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H Q
2601 GACTGGCTGA ATGCAAGGA GTACAAGTC AAGTCTCCA ACAAGCCCT CCCAGCCCC ATCGAGAAA CAATCTCAA AGCCAAAGG CAGCCCGGAG
CTGACCGACT TACGTTCT CATGTTACG TTCCAGAGT TGTTCGGGA GGTCGGGG TAGCTCTTTT GTTAGAGTT TCGGTTTCCC GTGCGGGCTC
339 D W L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R E
2701 AACACAGGT GTACACCCCTG CCCCATCCC GGAAGAGAT GACCAAGAAC CAGTCAAGC TGACCTGCCT GGTCAAAGG TTCTATCCCA GGCACATCGC
TTGTTGTCCA CATGTGGAC GGGGTAGG CCGTTCTCTA CTGTTCTCTA CTGTTCTCTA GTCCAGTCG ACTGGACGGA CCAGTTTCCG AAGATAGGT CGCTGTAGCG
373 P Q V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I A
2801 CGTGGAGTGG GAGACCAATG GGCAGCCGA GAACAATAC AAGACCAGC CTCCTGTGT GTACTCCGAC GGCTCCTTCT TCCTCTACAG CAAGCTCACC
GCACCTACC CTCTGTTAC CGTCCGCTT CTGTTGATG TTCTGTGCG GTCCAGTCG ACTGGACGGA CCAGTTTCCG AAGATAGGT CGCTGTAGCG
406 V E W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L T
2901 GTGACACAGA GCAGGTGGA GCAGGGGAAC GTCTTCTCAT GCTCCGTGAT GCATAGGCT CTGCACAACT ACTACACGCA GAAGAGCCTC TCCTGTCTC
CACCTGTTCT CGTCCACCGT CGTCCCTTG CAGAAGATA CGAGCATA CGTACTCCA GAGCTGTG TGATGTGGT CTCTCTGGAG AGGCACAGAG
439 V D K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S P
3001 CGGTAATAA AGCATCGAC GGCCTAGAG TCCTTAAGC TCGTTGCG CGGGGCTT TTTATTGTTA ACTCATGTTT GACAGCTTAT CATCGATAAG
GCCCATTTAT TCGTACGCTG CCGGATCTC AGGATTTGCG AGCCAAAGC GGCCTGCAA AATAACAAT TGAGTACAAA CTGTCAATA GTAGCTATT
473 G K O
3101 CTTTAAATGG GTAGTTTATC ACAGTTAAAT TGCTAAGCA GTCAAGCACC GTGTATGAA TCTAACAATG CGTCAATCGT CATCTCGG ACCGTACACC
GAAATTACG CATCAATAG TGTCAATTA ACGATTGGT CAGTCCGTG CACATCTT AGATTGTTAC GCGAGTAGCA GTAGGAGCCG TGGCAGTGG

FIG. 21D

3201 TGGATGCTGT AGCATAGGC TTGTTATGC CGTACTGCC GGCCTCTTG CGGATATCG TCCATTCCG CAGCATCGC AGTCACTATG GCGTCTGCT
ACCTAGACA TCCGTATCCG AACCAATAG GCCATGACG CCGGAGAAC GCCCTATAGC AGGTAAGGCT GTCGTAGCG TCAGTGATAC CGCAGGACGA

3301

FIG. 22A

1 GAATTCAACT TCTCCATACT TTGGATAAGG AAATACAGAC ATGAAAAATC TCATTGCTGA GTTGTATTTT AAGCTTGCCC AAAAAGAAGA AGAGTCGAAT
CTTAAGTTGA AGAGGTATGA AACCTATGCC TTTATGCTG TACTTTTAG AGTAACGACT CAACAATAAA TTCGAACGGG TTTTCTTCTT TCTCAGCTTA

101 GAACTGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAGG
CTTGACACAC GCGTCCATCT TCGAAACCTC TAATAGCAGT GACGTACGA AGGGTTATAC CGCGTTTAC TGGTTGTGCG CAACTAACCTA GTCCATCTCC

201 GGGCGCTGTA CGAGGTAAAG CCGATGCCA GCATTCTGA CGACATAGC GAGCTGCTGC GCGATTAGT AAAGAAGTTA TTGAAGCATC CTGCTCAGTA
CCCGGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA TTTCTTCAAT AACTTCGTAG GAGCAGTCAT

301 AAAAGTTAAT CTTTCAACA GCTGTCAATA AGTTGTCAGG GCCGAGACTT ATAGTCGCTT TGTTTTATT TTTTAATGTA TTGTAACTA GTACGCAAGT
TTTTCAATTA GAAAGTTGT CGACAGTATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA ACAAAAATAA AAAATTACAT AAACAATTGAT CATGCGTTCA

401 TCACGTAAA AGGGTATCTA GAATTATGAA GAAGATATC GCATTCTTC TTGCACTAT GTTCGTTTTT TCTATTGCTA CAAACGGTA CGCTGATATC
AGTGCATTTT TCCCATAGAT CTTAATACTT CTTCTTATAG CGTAAAGAAG AAGCTAGATA CAAGCAAAA AGATAACGAT GTTTGGCAT GCGACTATAG

1 M K K N I A F L L A S M F V F S I A T N A Y A D I
*STII Signal TIR -1 anti-VEGF Light Chain (1st generation)^

501 CAGATGACCC AGTCCCGCAG CTCCTGTGCC GCCTGTGG GGGATAGGTT CACCATCACC TGCAGCGCAA GTCAGATAT TAGCAACTAT TTAAACTGGT
GTCTACTGGG TCAGGGGCTC GAGGGACAGG CGGACACACC CGCTATCCCA GTGGTAGTGG ACGTCGCGTT CAGTCCCTATA ATCGTTGATA AATTGACCA

26 Q M T Q S P S S L S A S V G D R V T I T C S A S Q D I S N Y L N W Y

601 ATCAACAGAA ACCAGGAAA GCTCCGAAAG TACTGATTTA CTTACCTCC TCTCTCCACT CTGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC
TAGTTGTCTT TGGTCCCTTT CGAGGCTTTC ATGACTAAT GAAGTGGAGG AGAGAGGTGA GACCTCAGGG AAGAGCGAAG AGACCCTAGGC CAAGACCTG

60 Q Q K P G K A P K V L I Y F T S S L H S G V P S R F S G S G S G T

701 GGATTTCACT CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTGTC AAGTATAGC ACCGTGCCGT GGACGTTTG ACAGGGTACC
CCTAAGTGA GACTGGTAGT CGTCAGAGT CGGTCTTCTG AAGCGTTGAA TAATGACAGT TGTCTATCG TGGCAGCGCA CCGTCAACCC TGTCCTCATGG

93 D F T L T I S S L Q P E D F A T Y Y C Q Q Y S T V P W T F G Q G T

801 AAGTGGAGA TCAACGAAC TGTGGCTGCA CCATCTGCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT GTGTGCCCTGC
TTCCACCTCT AGTTTGCTTG ACACCGAGT GGTAGACAGA AGTAGAAGG CGGTAGACTA CTCGTCACT TTAGACCTTG ACGAAGACAA CACACGGACG

126 K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V V C L L

901 TGAATAACTT CTATCCAGA GAGGCCAAG TACAGTGAAG GGTGGATAAC GCCTCCAAT CGGTAACCTC CCAGAGAGT GTCACAGAGC AGGACAGCAA
ACTTATTGAA GATAGGTCT CTCCGGTTTC ATGTCACCTT CCACCTATTG CGGGAGTTA GCCCATTCAG GGTCTCTCA CAGTGTCTCG TCCTGTCTGTT

160 N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K

FIG. 22B

1001 GGACAGACC TACAGCCTCA GCAGCACCT GACCTGAGC AAAGCAGACT ACAGAAACA CAAAGTCTAC GCCTCGAAG TCACCCATCA GGGCCTGAGC
CCTGTCGTGG ATGTCGAGT CGTCGTGGG CTGCGACTCG TTTCGTCTGA TGCTCTTTGT GTTTCAGATG CGGACGCTTC AGTGGTAGT CCGGACTCG
193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S
1101 TCGCCGTCA CAAAGACTT CAACAGGGA GAGTGTAAAT TAAATCTCT AGCCCGAGC CATCGTGGC AGCTCGGTAC CCGGGATCT AGGCCTAACG
AGCGGCAGT GTTCTCGAA GTTGTCCTCT CTCACAATA ATTTAGGAGA TGGGGCCTGC GTAGCACCGC TCGAGCCATG GSCCCCTAGA TCCGGATTGC
226 S P V T K S F N R G E C O
1201 CTCGGTTGCC GCGGGCGTT TTTTATTGTT GCCGACGCG ATCTCGAATG AACTGTGTG GCAGTAGAA GCTTTGGAGA TTATCGTCA TGAATGCTT
GAGCAACG CGGCCCGCAA AAAATAACA CCGCTGCGG TAGAGCTTAC TTGACACACG CGTCCATCTT CGAAACCTCT AATAGCAGT ACCTTAGGAA
1301 CGCAATATG CGCAAAATGA CCAACAGCG TTGATTGATC AGGTAGAGG GCGGCTGTAC GAGGTAAAG CCGATGCCAG CATTCCTGAC GACGATACGG
GCGTTATACC GGGTTTACT GGTGTGCGC AACTAACTAG TCCATCTCC CCGGACATG CTCATTTTCG GGCTACGGTC GTAAAGACTG CTGCTATGCC
1401 AGCTGCTCG CGATTACGTA AAGAAGTTAT TGAAGCATCC TCGTCAGTAA AAGTTAATC TTTTCAACAG CTGTCAATAA GTTGTCACGG CCGAGACTTA
TCGACGACG GCTAATGCA TTTCTCAATA ACTTCGTAGG AGCAGTCAIT TTTCAATTAG AAAAGTTGTC GACAGTATTT CAACAGTGCC GGCTCTGAAT
1501 TAGTCGCTT GTTTTATTT TTTAATGAT TGTAACTAG TACGCAAGT CAGCTAAAA GGGTATCTAG AATTATGAAG AAGAATATCG CATTTCTTCT
ATCAGGAAA CAAAAATAA AAATTACATA AACATTGATC ATGCGTTCAA GTGCAITTTT CCATAGATC TTAATACCTT TTCTTATAGC GTAAAGAAGA
1 M K K N I A F L L
^STII Signal TIR-1
1601 TGCATCTATG TTGTTTCTT CTATTGCTAC AAACGCTAC GCTGAGTTC AGCTGGTGA GTCTGGCGGT GGCTGGTGC AGCCAGGGG CTCACCTCGT
ACGTAGATAC AAGCAAAAA GATAACGATG TTTGCGCATG CGACTCCAAG TCAGCCACCT CAGACCGCCA CCGGACCACG TCGTCCCCC GAGTGAGGCA
10 A S M F V F S I A T N A Y A E V Q L V E S G G L V Q P G G S L R
^anti-VEGF (1st generation) heavy chain
1701 TTGCTCTGT CAGCTTCTG CTATACCTTC ACCAATATG GTATGAATG GGTCCGTGAG GCCCGGGTA AGGGCTGGA ATGGTTGGA TGGATTAAAC
AACAGACAC GTCGAAGACC GATATGGAAG TGGTTGATAC CATACTGAC CCAGGCAGTC CCGGGCCCAT TCCCGACCT TACCCAACT ACCTAATGT
43 L S C A A S G Y T F T N Y G M N W V R Q A P G K G L E W V G W I N T
1801 CCTATACCG TGAACCGACC TATGCTGCGG ATTTCAAAG TCGTTTCACT TTCACTTTAG ACACCTCAA GTCCACAGCA TACCTGAGA TGAACAGCCT
GGATATGCC ACTTGGTGG ATAGCAGCC TAAAGTTTC AGCAAGTGA AAGTCGAATC TGTGAGGTT CAGCTGTCT ATGGACGTCT ACTTGTGCGA
77 Y T G E P T Y A A D F K R R F T F S L D T S K S T A Y L Q M N S L
1901 GCGTCTGAG GACACTGCC TCTATTACTG TGCAAGTAC CCCCATAIT ATGGGAGCAG CCACTGGTAT TTCGACGTCT GGGGTCAAG AACCTGGTC
CGCAGACTC CTGTGACGC AGATAATGAC ACGTTTCTAG GGGTGATAA TACCTCGTC GTGACCATATA AAGTGCAGA CCCAGTTC TTGGAGCCAG
110 R A E D T A V Y Y C A K Y P H Y Y G S S H W Y F D V W G Q G T L V
2001 ACCGTCTCCT CGGCCTCCAC CAAGGGGCCA TCGTCTTCC CCGTGCACC CTCTCCAAG AGCACTCTG GGGGCACAGC GGCCTGGGC TGCTGTGTC
TGGCAGAGA GCGGAGGTG GTTCCCGGT AGCAGAGG GGGACCTGG GAGGAGTTC TCGTGGAGC CCCCCTGTG CCGGGACCCG ACGGACCACT
143 T V S S A S T K G P S V F P L A P S S K S T S G G T A A L G C L V K

FIG. 22C

2101 AGGACTACTT CCCGAAACCG GTGACGGTGT CGTGAATCT AGGCGCCCTG ACCAGGGCG TGCACACCTT CCCGGCTGTC CTACAGTCCT CAGGACTCTA
TCCTGATGAA GGGGCTTGGC CACTGCCACA GCACCTTAG TCCGGGGGAC TGGTGGCCG ACCTGTGAA GGGCGACAG GATGTCAGGA GTCTGTGAT
177 D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S G L Y
2201 CTCCCTCAGC AGCGTGGTGA CTGTGCCCTC TAGCAGCTTG GGCACCCAGA CCTACATCTG CAAGTGAAT CACAACACCA GCAACACCA GGTGGACAAG
GAGGAGTCG TCGCACCACT GACACGGGAG ATCTCGAAT CCGTGGTCT GATGTAGAC GTTGCACCTA GTGTTCGGT GTTGTGGT CCACCTGTTC
210 S L S S V V T V P S S S L G T Q T Y I C N V N H K P S N T K V D K
2301 AAAGTTGAGC CCAATCTTG TGACAAACT CACATATGC CACCGTGCC AGCAGCTGAA CTCTGGGG GACCTGAGT CTCTCTTTC CCCCCAAAC
TTTCACTCG GGTTTAGAAC ACTGTTTGA GTGTGTACGG GTGGACGGG TCGTGACTT GAGGACCCCT CTGGCAGTCA GRAGGAGAG GGGGTTTGT
243 K V E P K S C D K T H T C P P C P A P E L L G G P S V F L F P P K P
2401 CCAAGGACAC CCTCATGATC TCCGGGACCC CTGAGTCTAC ATCGTGGTG GTGGACGTGA GCCACGAAGA CCCTGAGGTC AGTTCAACT GGTACGTGGA
GGTCTCTGT GGAGTACTAG AGGCGCTGG GACTCCAGT TACGCACCA CACTGTGACT CGGTGCTTCT GGGACTCCAG TTCAAGTTGA CCATGCACCT
277 K D T L M I S R T P E V T C V V V D V S H E D P E V K F N W Y V D
2501 CGGCGTGGAG GTGCATAATG CCAAGACAAA GCCGGGGAG GAGCAGTACA ACAGCAGCTA CCGTGTGTC AGCTCTCTCA CCGTCTGCA CCAGGACTGG
GCCGACCTC CAGTATTAC GGTCTGTTT CGGCGCCCTC CTCGTCATGT TGTGTCAT GTGCACAG GGCACACAG TCGCAGGAGT GGCAGGACGT GGTCTGACC
310 G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H Q D W
2601 CTGAATGGCA AGGAGTACAA GTGCAAGTCT TCCAAACAG CCCTCCAGC CCCATCGAG AATACCATCT CCAAGCCAA AGGGCAGCCC CGAGAACCAC
GACTTACCT TCCTCATGTT CAGGTTCCAG AGGTTGTTT GGGAGGTCG GGGTACTCT TTTTGTGAGA GTTTTCGGT TCCCGTCGG GCTCTTGGT
343 L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R E P Q
2701 AGGTGTACAC CTGCCCCCA TCOCGGGAAG AGATGACCAA GAACAGGTC AGCTGACCT GCCTGTGCAA AGGTTCTAT CCCAGCGACA TCGCCGTGGA
TCCCATGTG GGACGGGGT AGGCGCTTC TCTACTGTT CTGTGTCCAG TCGGACTGGA CGGACCACT TCCGAGATA GGTCTGCTGT AGCGCACCT
377 V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I A V E
2801 GTGGAGAGC AATGGGAGC CGGAGAACAA CTACAGACC AGCCTCCCG TGTGGACTC CGACGGCTCC TTCTTCTCT ACAGCAGCT CACGTTGAC
CACCTCTCG TTACCCGTCG GCCTCTTGT GATGTTCTG TCGGAGGGC ACAGCTGAG GCTCCGAGG AAGAAGGAGA TGTCTGTTCA GTGSCACCTG
410 W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L T V D
2901 AAGAGCAGT GGCAGCAGG GAACGTCTTC TCATGCTCG TGATGATGA GGCTCTGAC AACCACTACA CGCAGAAGAG CCTCTCCCTG TCTCCGGGTA
TTCTCGTCA CCGTCGTCCC CTTCAGAGAG AGTAGAGGC ACTAGTACT CCGAGACGTG TTGTTGATGT GGTCTTCTC GGAGAGGAC AGAGGCCAT
443 K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S P G K
3001 AATAGCATG CGACGGCCT AGATCCCTA AGCTCGGT GCGCGGGC GTTTTATT GTTAATCAT GTTTCACAG TTATCATCGA TAAGTTTAA
TTATTCTGAC GCTGCCGGA TCTCAGGAT TCGAGGCCA CCGCGGCCG CAAATAATA CAATGAGTA CAACTGTG AATAGTAGCT ATTGAAAT
477 O
3101 TCGGTGAGT TATCAGATT AATTTGCTAA CGCAGTCAG CACCGTGTAT GAAATCTAAC AATGCTCA TCGTATCTCT CGSCACCGTC ACCCTGGATG
ACGCCATCA ATAGTGTCAA TTTAACGATT GCGTCAGTCC GTGGACATA CTTAGATTG TTACCGAGT AGCAGTAGGA GCGGTGGCAG TGGACCTAC
3201 CTGTAGCAT AGGCTTGGT ATGCCGTTAC TGCCGGGCT CTTCGGGAT ATCGTCCATT CCGACAGCAT CGCCAGTAC TATGGGTGC TGTTAGCGCT
GACATCCGTA TCGAACCAA TAGGCCATG ACGGCCGGA GAAGCCCTA TAGCAGTAA GGCTGTGTA GGGTCACTG ATACCCGACG ACGATCGGA

FIG. 23A

>Anti-VEGF (VNERK version) IgG1 Expression Cassette with heavy chain FR1,2,3,4=consensus subgroupI

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ecori      pfIMI      bsrDI      hindIII      earI/ksp632I
1 GAATTCACCT TCTCCATCTT TTGGATAAGG AATATACAGC ATGAAAATC TCATTGCTGA GTTGTTATTT AAGCTTGCCC AAAAAGAAGA AGAGTCGAAT
CTTAAGTTGA AGAGGTATGA AACCTATTCC TTTATGTCTG TACTTTTAG AGTAAGCACT CACAAATAAA TTCGAACGGG TTTTCTTCT TCTCAGCTTA

      bspMI
      avIII/fspI      hindIII      bsrDI      bclI
101 GAATGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAGG
CTTGACACAC CGGTCCATCT TCGAAACCTC TAATAGCACT GACGTTACGA ACCGTTATAC CGCGTTTAC TGGTTGTGCG CAACTAACA GTCCATCTCC

      bsmI      snaBI
201 GGGCGCTGTA CGAGGTAAAG CCGCATGCCA GCATTCCTGA CGACATACG GAGCTGCTGC CGCATTCAGT AAAGAAGTTA TTGAAGCATC CTGCTCAGTA
CCCGCGACAT GCTCCATTTC GGCGTAGGGT CCGTAAGGACT GCTGCTATGC CTCGACGAGC GCGTAATGCA TTTCTTCAAT AACTTCGTAG GAGCAGTCAT

      ahdI/eam1105I
      pvuII      eagI/xmaIII/ec1XI      speI
301 AAAAGTTAAT CTTTTCACCA GCTGTCATAA AGTGTGCACG GCGGAGACTT ATAGTCGCTT TGTGTTTATT TTTTAATGTA TTTGTAACCTA GTAGCGCAAGT
TTTTCATTA GAAAAGTTGT CGACAGTATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA ACAAAATAA AAATATCAT AAACATGCT CATGCCGTTCA

      xbaI      bsiWI/splI      mluI      ecorV
401 TCACGTAAA AGGTATCTA GAATTATGAA GAACAATATC GCATTCTTC TTGCACTAT GTTCGTTTT TCTATTGCTA CAAACGCGTA CGCTGATATC
AGTGCATTTT TCCCATAGAT CTTAATACTT CTTCTTATAG CGTAAGAGAG AACGTAGATA CAAGCAAAA AGATAACGAT GTTTGGCAT GCGACTATAG
1 M K K N I A F L L A S M F V F S I A T N A Y A D I
^STII Signal TIR -1

      sstI      tth111I/aspI      sacI      pflPI      ecl136II      ecII      bstEII      bspMI      psi      ahaIII/draI
501 CAGTTGACCC AGTCCCGGAG CTCCCTGTCC GCTCTGTGG CGATPAGGT CACCATCACC TGCAGCGCAA GTCAGGATAT TAGCAACTAT TTAACCTGGT
GTCACCTGGG TCAGGGGCTC GAGGGACAGG CGGACACACC CGTATCCCA GTGGTAGTG ACCTCGGCTT CAGTCTATA ATCGTTGATA AATTGACCA
26 Q L T Q S P S S L S A S V G D R V T I T C S A S Q D I S N Y L N W Y

      scaI      bseRI      bpmI/gsuI      bamHI
601 ATCAACAGAA ACCAGGAAA GCTCCGAAAG TACTGATTA CTTCACTCC TCTCTCCACT CTGGAGTCCC TTCTGCTTC TCTGGATCCG GTTCTGGGAC
TAGTTGCTT TGGTCTTTT CGAGGCTTTC ATGACTAAT GAAGTGGAG AGAGAGTGA GACCTCAGG AAGAGCGAAG AGACCTAGGC CAAGACCTCG
60 Q Q K P G K A P K V L I Y F T S S L H S G V P S R F S G S G S G T

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FIG. 23B

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kpnI      asp718      acc65I
701 GGATTTCAC TGTGACCATCA GCAGTCTGCA GCCAGAGAGAC TTCGCAACTT ATTACTGTCA ACAGTATAGC ACCGTGCGGT GGACGTTTGG ACAGGGTACC
    CCTAAGTGA GACTGGTAGT CGTCAGACGT CGGTCTTCTG AAGCGTGAA TAATGACAGT TGTATATCG TGCACGGCA CCTGCAAAACC TGTCCTCATGG
93  D F T L T I S S L Q P E D F A T Y Y C Q Q Y S T V P W T F G Q G T

      bpuAI      xmnI      asp700
801 AAGGTGGAGA TCAAACGAAC TGTGGCTGCA CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT GTGTGCTGTC
    TTCCACCTCT AGTTTGCTTG ACACCGACGT GGTAGACAGA AGTAGAAGG CGGTAGACTA CTCGTCAACT TTAGACCTTG ACRAAGACAA CACACGGACG
126 K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V V C L L

      xmnI      asp700
901 TGAATAACTT CTATCCAGA GAGGCCAAG TACAGTGGAA GGTGGATAAC GCCCTCCAAT CGGTAACTC CCAGGAGAGT GTCACAGAGC AGACACAGAA
    ACTTATTGAA GATAGGTCT CTCCGGTTC ATGTCACTT CCACCTATTG CGGAGGTTA GCCCATTGAG GGTCTCTCA CAGTGTCTCG TCCTGTGTT
160 N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K

      cellI/espI      bspI      xmaI/pspAI
1001 GGACAGCACC TACAGCTCA GCAGCACCTT GAGCTGAGC AAGCAGACT AGCAGAAACA CAAAGTCTAC GCGTGAAG TCACCCATCA GGCCTGAGC
    CCTGTGCTGG ATGTGCGAGT CGTGTGGGA CTGCGACTCG TTTGCTCTGA TGCTCTTGT GTTTCAGATG CGGACGCTT AGTGGTAGT CCGGACTCG
193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S

      pacI      xmaI/pspAI
1101 TCGCCCGTCA CAAAGAGCTT CAACAGGGA GAGTGTAAAT TAAATCTCT AGCCGAGC CATCGTGGC AGCTCGGTAC CCGGGATCT AGCCTAACG
    AGCGGCAGT GTTCTCGAA GTTGTCCCT CTCACAATTA ATTTAGGAGA TCGGCGCTG GTAGCACCGC TCGAGCCATG GGGCCCTAGA TCCGGATTGC
226 S P V T K S F N R G E C O

      start lambda t0 terminator^

      bspMI      avIII/fspI      hindIII      bsrDI
1201 CTCGGTTGCC GCCGGCGTT TTTTATTGTT GCCGAGCGC ATCTCGAATG AACTGTGTG GCAGGTAGAA GCTTTGAGA TTATCGTCAC TGCAATGCTT
    GAGCAACGG CGGCCGCAA AAATAACAA CCGCTGGCG TAGACTTAC TTGACACAG CGTCCATCTT CGAAACCTCT AATAGCAGT ACCTTACGAA
      ^end lambda t0 terminator

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FIG.23C

1301 GCGAATATGG GCGAATATGA CCAACAGCGG TTGATTTGATC AGGTAGAGGG GCGCTGTAC GAGGTAAAGC CCGATGCCAG CATTCTGAC GACGATACGG
bclI bsmI
CGGTATATACC GCGTTTACT GGTGTGCGC AACTAATGAC TCCATCTGCC CCGGACATG CTCCATTGCG GGTACGGTC GTAAGGACTG CTGCTATGCC
1401 AGCTGCTGGG CCAATACGTA AAGAAGTTAT TGAAGCATCC TCGTCAGTAA AAGTTAATC TTTTCAACAG CTGTCAATAA GTTGTACCGG CCGAGACTTA
snaBI pvuII eagI/xmaII/eklXI
TCCAGCAAGC GCTAATGCAT TTCTTCAATA ACTTGTAGG AGCAGTCATT TTCAATTAG AAGGTGTG GACAGTATT CAACAGTGCC GGTCTGTGAT
1501 TAGTGCCTTT GTTTTATTT TTGATGAT TTGTAAGTAT TAGGCAAGTT CAGGTAAAA GGTATCTAG AATTATGAG AGAATATCG CATTCTTCT
xbaI
ATCAGCGAAA CAAAAATATA AATTACATA AACATTGATC ATGGGTTCAA GTGCAATTTT CCAATAGATC TTAATACTTC TTCTTATAGC GTAAAGAGA
M K K N I A P L L
*STII Signal TIR-1
1601 TGCATCTATG TTGTTTTT CTATTGCTAC AAGCGGTAC GCTCAGGTC AGCTGTGCA GTCTGGCGCA GAGGTAAAA AGCCAGGGGC TTCAGTTAAA
bsaNI/splI pvuII bsgI eco57I
ACGTAGATAC AAGCAAAAA GATACGATG TTGCGCATG CAGTCCAG TCGACCACT CAGACCGGT CTCCACTTTT TCGGTCCCG AGTCAATTT
10 A S M P V P S I A T N A Y A Q V Q L V Q S G A E V K K P G A S V K
*start xVEGF (VNERK) heavy chain (consensus subgroup I framework)
*FR1-SubgroupI
bsaNI/splI pvuII bsgI
1701 GTATCTCTGA AGCTTCTGG CTATGCTAC AAGCGGTAC GCTCAGGTC AGCTGTGCA GTCTGGCGCA GAGGTAAAA AGCCAGGGGC TTCAGTTAAA
xmaI/pspAI smaI alw261/bsmI
CATAGGACTT TTGAGAGACC GATATGGAAG TGGTTGATC CATATTTGAC CCAGGCAATC CCGGCGCCAG TCCCGGACCT TACCTACCTT ACCTAATGT
43 V S C K A S G Y T F T N Y G I N W V R Q A P G Q G L E W M G W I N T
*FR2-SubgroupI
1801 CCAATACCGG TAAACCGACC TATGCTGCGG ATTCAAAAG TGGTGTACT ATCACTGCTG ACACCTCCAC TAGCACAGCA TACATGGAAC TGTCTAGCCT
ageI
GGAATGGCC ACTTGGCTGG ATACGACGCC TAAAGTTGC AGCACAATGA TAGTGAGGAC TGTGAGGTG ATCGGTGCTG ATGTACCTTG ACAGATGGA
77 Y T G E P T Y A A D P K R R V T I T R D T S T S T A Y M E L S S L
*FR3-subgroupI
1901 GCGCTCTGAG GACACTGCGG TCTATTACTG TGCAGGTTAC CCGCACTATT ATGTGAACGA GCGAAGAGC CACTGGTATT TCGACGTCTG GGGTCAGGA
sapi earI/ksp632I aatII
CGCAAGACTC CTGTGACCGC AGATAATGAC AGGTGCAATG GCGGTATATA TACACTGCTG CCGCTTCTCG GTACACATAA AGCTGCACAC CCGAGTTCT
210 R S E D T A V Y Y C A R Y P H Y Y V N E R K S H W Y F D V W G Q G
FR4= same sequence for subgroupI, II and III

bseRI
esp3I
betEII bsmBI
2001 ACCCTGGTCA CGGTCTCTC GGCCTCCACC AAGGCCCAT CGGTCTTCCC CCTGGCACCC TCCTCCAGA GCACCTCTGG GGCACACGG GGCCTGGGCT
TGGACCAAGT GGCAGAGGAG CCGAGGTGG TTCCGGGTA GCCAGAAGG GAGCCGTGG AGAGGTCT CTGGAGACC CCGTGTGCG CGGACCCGA
143 T L V T V S S A S T K G P S V P L A P S S K S T S G G T A A L G C

bseRI
narl
kasi
ehel
2101 GCTGTGCA GACTACTTC CCGAACCGG TGACGGTGC GTGGAATCA GGGGCCCTGA CCAGCGGGT GCACACTTC CCGCTGTCTC TACAGTCTTC
CGACCAAGT CCGATGAG GGCCTGGCC ACTGCCACAG CACTTGAGT CGCGGGGACT GTGGCCGCA CGTGTGAAG GGCACACAG ATGTCAGGAG
177 L V K D Y P P E P V T V S W N S G A L T S G V H T P P A V L Q S S

narl
kasi
ehel
2201 AGGACTCTAC TCCTCAGCA GGTGGTGAC TGTGCCCTCT AGCAGCTGG GCACCCAGAC CTACATCTGC AACGTGATC ACAAGCCAG CAACACCAAG
TCCTGAGT AGGAGTCTT CGCACCACTG ACAGGGAGA TCGTGGACC CCGGTCTG GATGTAGAG TTGACTTAG TGTTCGGTC GTTGTGGTTC
210 G L Y S L S S V V T V P S S S L G T Q T Y I C N V N H K P S N T K

narl
kasi
ehel
2301 GTGACACAGA AAGTTGAGC CAATCTGT GACAACTC ACATGCCC ACCGTGCCA GCACCTGAC TCCTGGGGG ACCGTGCTC TTCTCTTCC
CACTGTCT TTCACTCG GTTAGACA CTGTTTAG TGTGACGG TGGACGGT CGTGACTTG AGGACCCCG TGCAGTCTG AAGAGAGG
243 V D K X V E P K S C D K T H T C P P C P A P E L L G G P S V P L P P

narl
kasi
ehel
2401 CCCCACAC CAGGACACC CTCATGATC CCGGACCC TGAGTCACTA TGGTGGTGG TGGAGTGG CCACAGAGC CTGAGGTCA AGTCAACTG
GGGTTTGG GTTCTGTGG GAGTACTAGA GGGCTGGG ACTCCAGTGT ACGCCACC ACCTGACTC GGTGCTTCTG GACTCCAGT TCAAGTTGAC
277 P K P K D T L M I S R T P E V T C V V V D V S H E D P E V K P N W

narl
kasi
ehel
2501 GTAGTGGAC GGTGTGAGG TGATATGC CAAGACAG CCGGGGAGG AGCAGTACA CAGCAGTAC CGTGTGGTCA GGTCTCTC CTTCTGAC
CATGCACTG CCGACCTCC AGTATTAC GTTCTGTTC GCGCCCTCC TCGTATGT GTCTGATG GCACACAGT CGCAGGAGT GCAGGAGTG
310 Y V D G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H

narl
kasi
ehel
2601 CAGGACTGGC TGATGGCA GAGTACAG TGCAAGTCT CCAACAAGC CCTCCAGC CCATCGAGA AACCATCTC CAAGCCAA GGCAGGCC
GTCTGAGC ACTTACGTT CTTATGTC AGTTTACAG GTTGTTCG GAGGAGTGG GGTAGCTCT TTGTTAGAG GTTCTGTTT CCGTGGGG
343 Q D W L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R

FIG.23D

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                xmaI/bspAI      smaI earI/ksp632I      sexAI      bspMI
2701 GAGAACACCA GGTGTACACC CTGCCCCCAT CCGGAGAGA GATGACCAAG AACAGGTCA GCTGACTG CCTGTCTATC CAGCGACAT
CTCTTGCTGT CCACATGTGG GACGGGGTA GGGCCTTCT CTACTGTTT TGGTCCAGT CGACTGAGC GACCAAGTTT CCGAAGATAG GGTGCTGTA
377 E P Q V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I

                bspDI
2801 CGCCTGGAG TGGAGAGCA ATGGGAGCC GGAGAACAC TACAGACCA CGCCTCCGT GCTGACTCC GACGGCTCT TCTTCTCTA CAGCAGCTC
GGGACCTC ACCCTCTGT TACCGTCCG CTCTTGTG ATGTTCTGT GGGAGGGA CGACTGAG CTGCCAGGA AGAAGGAGT GTCTTCGAG
410 A V E W E S N G Q P E N N Y K T T P P V L D S D G S F P L Y S K L

                bpuAI      xmaI bbsI      asp700      nsII/avaIII bspI      sapI      earI/ksp632I
2901 ACCGTGACA AGACAGGTG GCAGCAGGG AACGTCTCT CATGCTCTT CATGCTGAG GCTGACACA ACCACTACAC GCAGAGAGC CTCTCCCTGT
TGGACCTGT TCTGTCCAC CTGTGTCCT TGCAGAGA GTACGAGGA CTACGTACTC CGAGAGCTGT TGGTATGTG CGTCTTCTG GAGAGGACA
443 T V D K S R W Q Q G N V P S C S V M H E A L H N H Y T Q K S L S L S

                sphI      hpaI      claI/bsp106      bspDI
3001 CTCGGGTAA ATAAGCATG CACGGCCTA GATGCTTAA CGTCGGTGG CGCGGGGG TTTTATTG TTAAGTATG TTGACAGCT TATCATGAT
GAGGCCAT TATGTTACG CTGCGGAT CTGAGGAT GCGAGCAAC GCGGCCCG AAAAAATAC AATGATGAC AAATGTGCA ATAGTAGCTA
477 P G K O

                *lambda to terminator

                hindIII
3101 CTCGGTAAAT CGGTAGTTT ATCAGATTA ATTGCTAAC GCAGTCAGC ACCGTGATG AAATCTACA ATGCGCTCAT GGTATCTC GGCACCGTCA
TTGAAATTA CGCCATCAA TAGTGTCAAT TTAAGATTG CGTCAGTCC TGGACATAC TTAGATTGT TACGCGAGTA GCAGTAGGAG CCGTGGCAGT

                ecorV
3201 CCTGGATGC TGTAGGATA GGCTTGGTA TGGCGTACT GCGGGGCTC TTGGGGATA TGCTCCATC CGACAGCAT GCCAGTCACT ATGGGCTGCT
GGGACCTAG ACATCGTAT CGAACCAAT ACGCCCAT GCGGCCGAG AAGCCCTAT AGCAGTAA GCTGTCTAG CCGTCAGTGA TACCGACGA
3301

> length: 3300
aatII (GAGTC): 1983
acc65I (GGTACC): 795 1176
ageI (ACCGT): 1806 2126
abaIII (TTTAA): 590
abaI (GACNNNGTC): 346 1495 2380
alw26I (CAGNNCTG): 1089 1770 2359
alw44I (GTGCAC): 1930 2169

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FIG. 23E